Archives of Neurology and Psychiatry

VOLUME 33 JANUARY 1935 NUMBER 1

INSULIN HYPOGLYCEMIA

MECHANISM OF THE NEUROLOGIC SYMPTOMS

WILLIAM DAMESHEK, M.D.
AND
ABRAHAM MYERSON, M.D.
WITH THE TECHNICAL ASSISTANCE OF
CAROLINE STEPHENSON, A.B.
BOSTON

Perhaps the most interesting of the symptoms of the insulin reaction are those related to the central nervous system. These have been well described by many authors.[1] At first there is a sense of weakness, a vague feeling of uneasiness. Then follow in rapid succession vertigo, ataxia, mental confusion, incoherence of speech and marked coarse tremor. Clonic spasms and even convulsions may supervene. The last stage of the reaction, if it is allowed to continue, is complete unconsciousness. Although there has been some speculation regarding the nature of these severe symptoms, very little concerning their mechanism has been established.

It was thought that the "internal jugular method" developed by one of us (A. M.[2a]) might help to elucidate the problem. Puncture of the internal jugular vein in man was undertaken in 1927 in the hope that greater knowledge regarding intracranial activity or metabolism might thus be obtained. Simultaneous puncture of the common carotid artery, internal jugular vein, brachial artery and basilic vein, with subsequent determination of the contents of oxygen, carbon dioxide and dextrose, proved valuable in the comparison of metabolic activity within the brain with that in the muscles of the arm.[2b] It was found that the difference in dextrose content between the carotid artery and the internal jugular vein was definitely greater than that between the brachial artery and the basilic vein. A similar difference, somewhat

Read before the Boston Society of Neurology and Psychiatry, Oct. 4, 1933.

From the Division of Research, Boston State Hospital and the Department of Neurology, Tufts College Medical School.

1. (*a*) Carr, A. D.: Neurologic Syndromes Associated with Hypoglycemia, J. A. M. A. **97**:1850 (Dec. 19) 1931. (*b*) Bowen, B. D., and Beck, G. M.: Insulin Hypoglycemia: Two Cases with Convulsions; One Necropsy Report, Ann. Int. Med. **6**:1412 (May) 1933.

2. (*a*) Myerson, A.; Halloran, R. D., and Hirsch, H. L.: Technic for Obtaining Blood from the Internal Jugular Vein and the Internal Carotid Artery, Arch. Neurol. & Psychiat. **17**:807 (June) 1927. (*b*) Myerson, A., and Halloran, R. D.: Studies of the Biochemistry of the Brain Blood by Internal Jugular Puncture, Am. J. Psychiat. **10**:389, 1930.

less in degree, was found in the arteriovenous contents of oxygen. From these results it was possible to speculate that the brain utilizes more sugar and probably more oxygen than do the muscles of the forearm. It has thus been possible to study indirectly some of the features of intracranial metabolism.

METHODS AND MATERIAL

Patients of the Boston State Hospital were used.[3] Young or middle-aged patients whose condition was diagnosed as dementia praecox were usually taken, although occasionally a patient with dementia paralytica was utilized. These patients presented no abnormalities except those referable to the mental condition; numerous studies of the urine and of the chemical constituents of the blood gave results that were within normal limits. The patients came to the operating room in the morning after a twelve hour fast. Following a preliminary period of rest, the neck in the region of the tip of the mastoid process was cocainized. Punctures by three operators were then made of (1) the brachial artery at the bend of the elbow,[4] (2) the internal jugular vein and usually (3) one of the basilic veins. In most instances punctures were made simultaneously; occasionally there was a delay of several seconds between punctures. Whenever difficulty was encountered in puncturing a vessel or when the time between punctures was delayed more than two minutes, the results were not utilized. Blood was collected in oil-coated syringes and transferred under oil to test tubes. Insulin was then injected intravenously in doses ranging from 8 to 80 units. At the height of the reaction, which occurred in from thirty to sixty minutes after the injection of insulin, samples of blood were again withdrawn from the aforementioned vessels. In certain experiments several samples were removed at different intervals; in these cases the needle, which had been plunged into the jugular vein, was frequently kept in situ for from thirty to sixty minutes.

The pulse rate and blood pressure were observed at frequent intervals. Observations of the degree of perspiration, tremor and general behavior of the patient were made, particular attention being paid to such features as tremor, twitching of the muscles and size of the pupils. In a number of patients the spinal fluid pressure was measured throughout the course of the experiment; in these instances the spinal fluid sugar was also estimated. Occasionally, the internal jugular venous pressure was determined by the method of Myerson and Loman.[5] A few experiments were performed in which the effect of epinephrine as superimposed on that of insulin was noted.

Most experiments were completed within forty-five minutes after the first samples of blood had been withdrawn. In a few instances, a period of from sixty to ninety minutes was necessary. At the end of the experiment the patient was given about 25 Gm. of dextrose either by mouth or intravenously (in 50 per cent solution) if the reaction was severe.

---

3. Dr. James V. May, superintendent of the Boston State Hospital, and his staff extended many courtesies in connection with this work.

4. Numerous comparisons during the course of two years between the blood of the carotid and that of the brachial artery failed to disclose any significant variation in the clinical constituents; puncture of the internal carotid artery was therefore discarded.

5. Myerson, A., and Loman, J.: Internal Jugular Venous Pressure in Man: Its Relationship to Cerebrospinal Fluid and Carotid Arterial Pressures, Arch. Neurol. & Psychiat. **27**:836 (April) 1932.

The blood sugar was estimated by the method of Folin and Wu,[6] two separate determinations being made on each sample. To avoid glycolysis, the protein-free filtrate was obtained within ten minutes after blood had been withdrawn. A series of comparisons between the Folin-Wu and the Benedict[7] method was made during one stage of this investigation. The oxygen content, oxygen capacity and carbon dioxide content of the blood were determined by the method of Van Slyke and Neill,[8] duplicate determinations on separate machines always being made. The lactic acid content of the blood was determined by the method of Friedemann, Cotonio and Shaffer.[9]

Following is a protocol of a patient with a typical severe reaction:

A. F., April 20, 1932.

8:55 a.m.: Blood from the brachial artery and internal jugular vein taken simultaneously; internal jugular venous pressure obtained. Spinal puncture made and 5 cc. of spinal fluid withdrawn; spinal fluid pressure obtained. Pulse rate, 132; arterial blood pressure, 120 systolic and 80 diastolic. Spinal fluid pressure, 210 mm. of spinal fluid. Internal jugular venous pressure, 110 mm. of venous blood. Blood sugar, brachial, 94 mg. per hundred cubic centimeters; internal jugular, 86 mg. Oxygen content, brachial, 20.3 per cent volumes per hundred cubic centimeters; internal jugular, 15.7 per cent.

9:00 a.m.: Spinal fluid pressure, 180 mm. Internal jugular venous pressure, 110 mm. Insulin, 80 units, given intravenously.

9:15 a.m.: Pulse rate, 116; arterial blood pressure, 110 systolic and 64 diastolic. Spinal fluid pressure, 150 mm. Internal jugular venous pressure, 60 mm.

9:24 a.m.: Pulse rate, 104; arterial blood pressure, 100 systolic and 58 diastolic. Spinal fluid pressure, 108 mm.

9:26 a.m.: Spinal fluid pressure, 210 mm.

9:29 a.m.: Spinal fluid pressure, 255 mm. Internal jugular venous pressure, 140 mm. Patient beginning to perspire.

9:34 a.m.: Pulse rate, 100; arterial blood pressure, 110 systolic and 44 diastolic. Spinal fluid pressure, 270 mm. Blood sugar, brachial, 33 mg. per hundred cubic centimeters; internal jugular, 26 mg. Oxygen content, brachial, 20.8 per cent; internal jugular, 17.6. Profuse perspiration; limpness of muscles; coarse tremor. Brachial and internal jugular blood taken.

9:37 a.m.: Extreme tremor; convulsive twitchings. Spinal fluid needle removed.

9:42 a.m.: Brachial and internal jugular blood taken.

---

6. Folin, Otto, and Wu, H.: A System of Blood Analysis: I. J. Biol. Chem. **38**:106, 1919; Supplement I. A Simplified and Improved Method for the Determination of Sugar, ibid. **41**:367, 1920.

7. Benedict, S. R.: The Analysis of Whole Blood: II. The Determination of Sugar and of Saccharoids (Non-Fermentable, Copper Reducing Substances), J. Biol. Chem. **92**:141, 1931.

8. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in the Blood and Other Solutions by Vacuum Extraction and Manometric Measurements, J. Biol. Chem. **51**:523, 1924.

9. Friedemann, T. E.; Cotonio, Margaret, and Shaffer, P. A.: The Determination of Lactic Acid, J. Biol. Chem. **73**:335, 1927.

10:00 a. m.: Patient vomited. Marked convulsive twitchings; skin cold and clammy. Patient given 25 cc. of dextrose in 50 per cent solution intravenously.

RESULTS

Insulin Reaction.—The onset of the reaction usually took place thirty minutes after the injection of insulin, when perspiration began. Shortly thereafter, tremor of the hands became visible, rapidly becoming more marked. With a severe reaction, spastic movements of the fingers and then of the arms became visible. Occasionally, jerky movements of the entire body were seen. Severe reactions were terminated by the intravenous injection of dextrose before a possible convulsion could supervene. At the end of the reaction the entire body became limp and the muscles seemed very flabby. One patient fell asleep (coma?); another patient became unconscious and almost fell from the operating table. This patient, with catatonic dementia praecox, who had never previously been observed either to speak or to smile, began to talk volubly and to smile directly after this episode and for a few minutes after the intravenous administration of dextrose. The pupils were observed carefully in several experiments. At no time was dilatation observed; in fact, constriction usually occurred. The reactions, which varied markedly in different patients and at different times in the same patient, may be classified as absent, slight, moderate and marked. The slight reactions were characterized by slight perspiration, a coarse, rapid tremor and slight limpness of muscles occurring toward the end of the reaction. The moderate reaction was characterized by marked perspiration, marked tremor and moderate limpness of muscles. The marked reaction (type 3 of tables 2 and 3) was characterized by profuse perspiration, marked tremor, twitching of muscles, marked limpness of muscles and at times coma.

Blood Sugar (table 1 and charts 1 and 2).—Before the administration of insulin the brachial-jugular difference in dextrose content varied from 2 to 21 mg. per hundred cubic centimeters in the various subjects. The difference of only 2 mg. in patient H. B. was exceptional in that all the other patients showed a difference of at least 7 mg. between the brachial artery and the jugular vein. The average brachial-jugular difference in the twenty-three patients was 11.2 mg. per hundred cubic centimeters. The brachial-basilic difference in dextrose content was distinctly less, the variation being from no difference to 9 mg., the average difference being 5.3 mg. These results correspond closely with those obtained in several hundred determinations in the past, as well as with the results of Lennox,[10] who used the same method in certain studies.

10. Lennox, W. G.: The Cerebral Circulation: XIV. The Respiratory Quotient of the Brain and of the Extremities in Man, Arch. Neurol. & Psychiat. **26**:719 (Oct.) 1931.

TABLE 1.—*The Blood Sugar and the Arteriovenous Differences in Dextrose Content Before and After the Administration of Insulin*

Patient	Determination	Insulin, Units	Blood Sugar, Mg. per 100 Cc.															
			Brachial Artery				Internal Jugular Vein				Basilic Vein		Brachial-Jugular Difference				Brachial-Basilic Difference	
				After				After						After				
			Before	1	2	3	Before	1	2	3	Before	After	Before	1	2	3	Before	After
R. B.	1	34	97	83	..	..	90	69	..	..	97	82	7	14	..	..	0	1
H. B.	1	80	89	72	..	..	87	66	..	..	..	..	2	6	..	..	..	..
W. E.	1	20	130	46	..	..	109	41	..	..	121	48	21	5	..	..	9	0
W. B.	1	16	101	57	..	..	87	49	..	..	93	45	14	12	..	..	8	8
W. B.	2	30	99	39	56	..	89	33	48	..	..	..	10	6	12	..	..	..
A. F.	1	25	101	59	..	..	89	50	..	..	96	50	12	9	..	..	5	9
M. G.	1	34	101	56	..	..	94	48	..	..	96	48	7	8	..	..	5	8
J. H.	..	32	123	46	..	..	111	43	..	..	118	47	12	3	..	..	5	—1
A. McN.	..	64	99	59	62	..	87	55	52	..	..	..	12	4	10	..	..	..
E. B.	1	18	106	56	..	..	91	39	..	..	104	43	15	17	..	..	2	13
E. B.	2	60	98	49	..	..	89	46	..	..	..	..	9	3	..	..	..	..
W. E.	2	40	132	55	62	..	121	38	65	..	..	..	11	17	3	..	..	..
M. G.	2	8	110	50	..	..	96	44	..	..	101	40	14	6	..	..	9	10
M. G.	3	26	105	52	..	..	89	45	..	..	99	45	16	7	..	..	6	13
T. O'B.	1	16	95	48	..	..	82	39	..	..	92	41	13	9	..	..	3	7
T. O'B.	2	72	95	53	48	47	84	42	41	40	..	..	11	11	7	7	..	..
E. B.	3	60	92	46	..	..	85	35	..	..	..	..	7	11	..	..	..	..
R. B.	2	20	105	49	..	..	95	42	..	..	101	41	10	7	..	..	4	8
A. Fr.	..	50	97	55	..	..	84	47	..	..	96	49	13	8	..	..	1	6
H. H.	..	56	102	53	..	..	93	47	..	..	..	..	9	6	..	..	..	..
T. A.	..	80	82	34	44	42	70	30	34	35	..	..	12	4	10	7	..	..
R. B.	3	30	115	34	38	..	103	31	33	..	..	..	12	3	5	..	..	..
H. B.	2	26	104	38	..	..	95	32	..	..	97	31	9	6	..	..	7	7
A. F.	2	80	94	33	44	..	86	26	36	..	..	..	8	7	8	..	..	..

TABLE 2A.—*The Oxygen Content and Arteriovenous Differences in Oxygen Content Before and After Administration of Insulin*

Patient	Determination	Insulin, Units	Lowest Blood Sugar, Mg. per 100 Cc.	Oxygen Content, Vols. per 100 Cc.															
				Brachial Artery				Internal Jugular Vein				Basilic Vein		Brachial-Jugular Difference				Brachial-Basilic Difference	
					After				After						After				
				Before	1	2	3	Before	1	2	3	Before	After	Before	1	2	3	Before	After
R. B.	1	34	69	20.1	19.0	....	....	12.6	11.7	....	....	12.5	12.6	7.5	7.3	...	...	7.7	6.4
H. B.	1	80	66	20.7	20.9	....	....	14.7	13.9	....	....	....	....	6.0	7.0	...	...	...	...
W. E.	1	20	41	18.3	17.8	....	....	11.8	10.3	....	....	12.7	11.4	6.5	7.5	...	...	5.6	6.4
W. B.	1	16	45	16.4	17.7	....	....	11.3	14.0	....	....	6.4	9.2	5.1	3.7	...	...	10.0	8.5
W. B.	2	60	33	16.4	17.5	16.7	....	11.3	11.3	12.0	....	....	....	5.1	6.2	4.6	...	...	...
A. F.	1	26	46	18.0	18.0	....	....	12.5	12.5	....	....	13.5	13.5	5.5	5.5	...	...	4.5	4.5
M. G.	1	34	48	21.6	21.8	....	....	13.6	14.0	....	....	15.1	16.8	8.0	7.8	...	...	6.5	5.0
J. H.	..	32	43	20.6	20.3	....	....	14.1	14.1	....	....	16.6	14.2	6.5	6.2	...	...	4.0	6.1
A. McN.	..	64	55	21.1	21.2	20.1	....	14.2	15.8	13.8	....	....	....	6.9	5.4	6.3	...	...	...
E. B.	1	18	39	19.1	18.9	....	....	10.6	12.1	....	....	12.6	16.4	8.5	6.8	...	...	6.5	2.5
E. B.	2	60	49	20.7	21.7	....	....	14.7	16.2	....	....	....	....	6.0	5.5	...	...	...	...
W. E.	2	40	38	19.4	18.4	18.1	....	14.2	12.4	11.7	....	....	....	5.2	6.0	6.4	...	...	...
M. G.	2	8	40	19.6	20.0	....	....	13.8	14.5	....	....	13.7	14.7	5.8	5.5	...	...	5.9	5.3
M. G.	3	26	43	20.3	19.5	....	....	12.2	14.5	....	....	15.6	14.0	8.1	5.0	...	...	4.7	5.5
T. O'B.	1	16	39	19.0	19.0	....	....	11.7	13.6	....	....	17.0	15.7	7.3	5.4	...	...	2.0	3.3
T. O'B.	2	72	40	20.2	20.1	18.8	18.2	14.6	15.5	14.0	13.3	....	....	5.6	4.6	4.8	4.9	...	...
E. B.	3	60	40	20.1	20.0	....	....	13.6	15.5	....	....	....	....	6.5	4.5	...	...	...	...
R. B.	2	20	41	18.5	17.7	....	....	11.5	14.4	....	....	11.4	11.6	7.0	3.3	...	...	7.1	6.1
A. Fr.	..	50	47	20.0	17.7	....	....	13.3	14.3	....	....	14.0	15.5	6.7	3.4	...	...	6.0	2.2
H. H.	..	56	40	20.8	21.5	....	....	15.8	16.2	....	....	....	....	5.0	5.3	...	...	...	...
T. A.	..	80	30	21.2	20.3	20.5	18.2	10.6	13.9	11.7	12.7	....	....	10.6	6.4	8.8	5.5	...	...
R. B.	3	30	31	19.1	19.2	18.5	....	13.9	15.2	15.3	....	....	....	5.2	4.0	3.0	...	...	...
H. B.	2	26	31	19.2	19.7	....	....	14.3	16.9	....	....	13.6	16.0	4.9	2.8	...	...	5.6	3.7
A. F.	2	80	26	20.3	20.8	20.1	....	15.7	17.6	16.4	....	....	....	4.6	3.2	3.7	...	...	...

Following the administration of insulin, the difference in dextrose content between the brachial artery and the jugular vein usually became diminished. In the group of severely reacting patients, numbering seven, the brachial-jugular difference in dextrose content before insulin was administered averaged 10.4 mg., whereas after the administration of insulin it averaged 5.8 mg. per hundred cubic centimeters. This

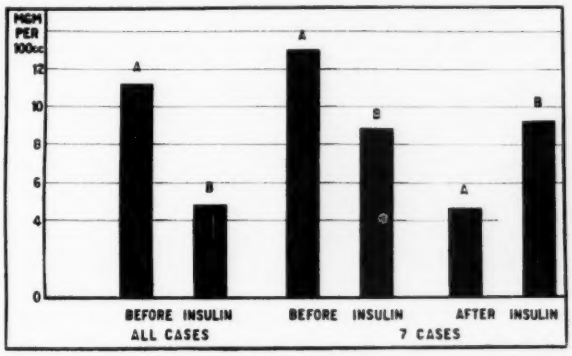


Chart 1.—Arteriovenous differences in the dextrose content of the blood before and after the administration of insulin (average figures) in seven severely reacting patients: *A*, brachial-jugular difference; *B*, brachial-basilic difference.

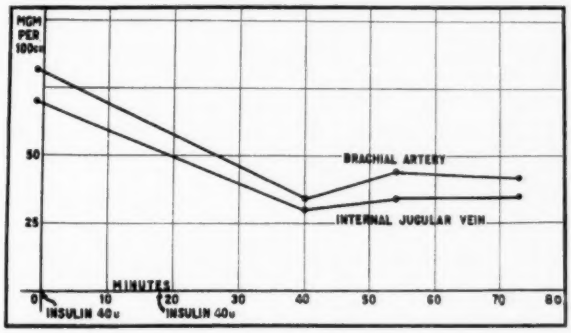


Chart 2.—Arteriovenous differences in the dextrose content of the blood (brachial minus jugular content) in a patient reacting severely to 80 units of insulin. Note the diminution in the brachial-jugular difference in the dextrose content at forty and seventy-five minutes.

may be contrasted with the findings in the brachial artery and basilic vein in seven patients reacting either moderately or markedly to insulin; the average arteriovenous difference before insulin was given was 4.6 mg. but after the administration of insulin it became increased to 9.1 mg. The possible reasons for these contrasting results will be noted in the comment.

Oxygen Content (table 2 and charts 3 and 4).—Before the administration of insulin the brachial-jugular difference in oxygen content varied from 4.6 to 10.6 volumes per hundred cubic centimeters; the brachial-basilic difference, from 2 to 9.6 volumes. The average of the twenty-three brachial-jugular differences in oxygen content was 6.4 volumes, that of the brachial-basilic differences being somewhat less—5.8 volumes. The slightly greater oxygen uptake by the brain than by the arm under normal conditions had been observed by us in our previous investigations and by Lennox.[11]

TABLE 2B.—*The Oxygen Saturation and the Percentage of Diminution in Oxygen Uptake by the Arm and the Brain Before and After the Administration of Insulin*

		Oxygen Saturation, per Cent								Percentage of Diminution in Oxygen Uptake		Average per Cent of Diminution in Brain	Reaction Type
	Determination from Table	Brachial Artery			Internal Jugular Vein			Basilic Vein					
			After			After							
Patient	2A	Before	1	2	Before	1	2	Before	After	Arm	Brain		
R. B.	1	99	93	..	62	58	..	61	62	17	3	....	0
H. B.	1	95	95	..	67	63	..	..	..	..	(17)*	....	0
W. E.	1	96	93	..	62	59	..	67	60	(14)	(15)	0	0
W. B.	1	93	99	..	64	79	..	36	52	15	27	....	1
W. B.	2	93	99	94	64	64	68	..	..	..	10	....	1
A. F.	1	96	96	..	66	66	..	72	72	0	0	....	1
M. G.	1	96	97	..	60	64	..	67	74	23	3	....	1
J. H.	..	98	96	..	67	67	..	79	67	(52)	5	....	1
A. McN.	..	99	99	94	56	74	64	..	..	..	22	11.2	1
E. B.	1	95	94	..	53	60	..	63	82	62	20	....	2
E. B.	2	95	99	..	67	74	..	..	..	..	8	....	2
W. E.	2	98	94	93	73	63	60	..	..	..	(15)	....	2
M. G.	2	96	97	..	67	71	..	67	72	10	5	....	2
M. G.	3	95	92	..	57	68	..	73	66	(17)	38	....	2
T. O'B.	1	93	92	..	57	66	..	83	76	(7)	26	....	2
T. O'B.	2	99	99	90	72	76	65	..	..	..	18	....	2
E. B.	3	95	94	..	64	73	..	..	..	..	31	16.4	2
R. B.	2	95	91	..	59	74	..	58	59	14	53	....	3
A. Fr.	..	99	88	..	66	70	..	69	77	63	49	....	3
H. H.	..	94	97	..	71	73	..	..	..	..	(6)	....	3
T. A.	..	97	93	84	49	64	58	..	..	..	48	....	3
R. B.	3	98	99	95	72	78	80	..	..	..	42	....	3
H. B.	2	91	93	..	67	80	..	64	75	34	43	....	3
A. F.	2	95	97	94	73	82	77	..	..	..	30	37.0	3

* The value in parentheses indicates an increase rather than a diminution in oxygen uptake.

After the administration of insulin the oxygen uptake by the brain (brachial-jugular difference in oxygen content[12]) varied with the degree of reaction. Thus, in the patients without appreciable reaction, there was no diminution in oxygen uptake; in the slightly reacting ones the oxygen uptake averaged 11.2 per cent less than before insulin; in the moderately reacting ones it was 16.4 per cent less, while in the severely

11. Lennox, W. G.: The Oxygen and Carbon Dioxide Content of Blood from the Internal Jugular and Other Veins, Arch. Int. Med. **46**:630 (Oct.) 1930. Lennox.[10]

12. Whether the difference in content of a metabolite between an artery and a vein can be said to be due to the use of that metabolite by the tissues in a given site is open to question. This is taken up at some length in the comment.

reacting patients it was 37 per cent less than before insulin was given.[13] About the same results held true for the forearm; in the presence of a moderate reaction, the oxygen uptake was diminished 12.5 per cent; in that of a severe reaction, 37 per cent.

Carbon Dioxide Content.—After the administration of insulin the difference in carbon dioxide content between the internal jugular vein and the brachial artery became diminished according to the extent of

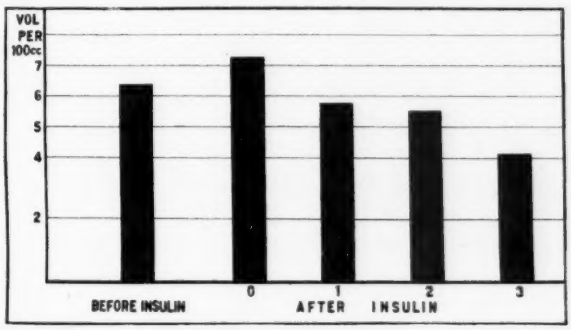


Chart 3.—Arteriovenous differences in the oxygen content (brachial minus jugular content) before and after the administration of insulin: *0,* no reaction; *1,* slight reaction; *2,* moderate reaction; *3,* marked reaction.

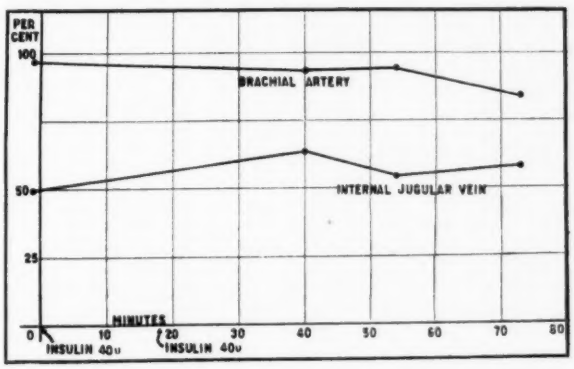


Chart 4.—The oxygen saturation of the blood in the brachial artery and internal jugular vein in a patient reacting severely to 80 units of insulin. Note the gradual "arterialization" of the jugular blood while the oxygen saturation of the brachial blood was becoming diminished. This might indicate a deficient uptake of oxygen by the brain during insulin hypoglycemia.

the reaction, and varied directly with the arteriovenous differences in oxygen content.

13. Patient H. H., although presenting a severe reaction, showed no diminution in oxygen uptake. If the case of H. H. had been discarded, the average diminution in oxygen uptake would have been 44.1 per cent.

Lactic Acid Content.—There was essentially no difference in lactic acid content between the different vessels either before or after the administration of insulin, although the lactic acid content became increased at the height of the reaction. The degree of increase did not bear any definite relationship to the type of reaction.

Spinal Fluid (table 3 and chart 5).—The cerebrospinal fluid was studied in eleven cases. In ten cases the pressure was measured during the time of the experiment. In each instance the spinal fluid pressure became increased following the administration of insulin. The increase in pressure usually occurred before any visible reaction, such as perspiration or tremor, could be seen, and took place from nineteen to thirty-one minutes after insulin had been given. Wide fluctuations in pressure

TABLE 3.—*The Spinal Fluid Before and After the Administration of Insulin*

Patient	Insulin, Units	Venous Blood Sugar, Mg. per 100 Cc.		Spinal Fluid Sugar, Mg. per 100 Cc.		Spinal Fluid Pressure, Mm. Water		Time at Which Rise in Spinal Fluid Pressure, Occurred, Min. After Injection		Reaction Type
		Before	After	Before	After	Before	Peak	Beginning Rise	Peak	
H. B.	80	87	66	77	77	140	200	22	36	0
W. B.	20	103	60	61	62	30	120	21	34	1
A. McN.	64	87	55	58	58	...	...	..	..	1
E. B.	60	89	46	56	56	100	230	28	30	2
M. G.	32	100	39	60	56	85	240	24	28	2
A. F. (1)	60	88	42	..	..	90	170	19	24	2
T. O'B.	16	82	39	57	57	...	...	..	..	2
W. E.	40	121	65	73	73	...	...	..	..	2
A. F. (2)	50	96	49	57	58	80	135	20	27	3
E. B.	60	85	35	..	..	110	250	31	42	3
H. H.	56	93	40	58	56	150	220	22	29	3
T. A.	80	70	30	51	55	...	...	..	..	3
R. B.	30	103	31	72	72	145	280	25	38	3
A. Fr.	80	86	26	48	52	170	270	24	34	3

were noted at the beginning of the spinal fluid "reaction" to insulin. Within from two to fourteen minutes thereafter the pressure was at its peak. The greatest rises were noted in the most severely reacting patients. In a few cases the pressure within the internal jugular vein was obtained simultaneously with that of the spinal fluid. The intrajugular pressure in these cases became definitely, though slightly, increased simultaneously with the increase in spinal fluid pressure.

The spinal fluid content of dextrose during the usual period of observation (from forty-five to ninety minutes) did not become diminished. Observations by other investigators on animals have shown that a distinct drop in spinal fluid sugar does not take place for two and one-half hours after the administration of insulin.[14]

14. Kasahara, M., and Uetani, E.: The Effect of Insulin upon the Reducing Substance in the Cerebrospinal Fluid of Normal Animals, J. Biol. Chem. **59**:433. 1924.

In a case of dementia paralytica with increased total protein and a colloidal gold curve typical of this disease, there was no change in these observations after insulin had been given.

Arterial Blood Pressure and Pulse Rate.—In fourteen cases, the arterial blood pressure during the course of the experiment was determined. The systolic pressure usually remained the same, although in four cases there was definite, though slight, increase (from 12 to 16 mm. of mercury). The diastolic pressure usually became diminished, the diminution varying from 10 to 36 mm. The pulse pressure thus became increased, definite elevation being noted in nine of the fourteen

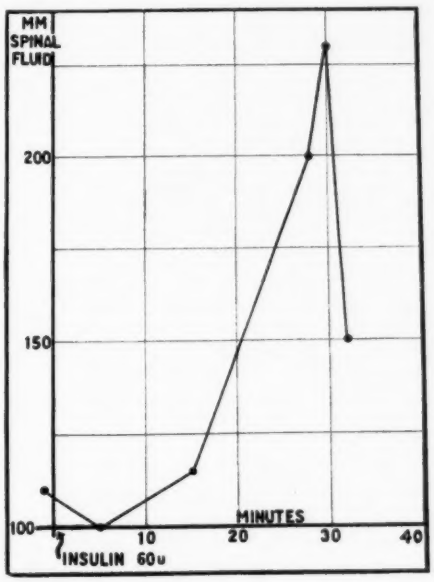


Chart 5.—The behavior of the spinal fluid pressure during insulin hypoglycemia. The pressure begins to rise before visible reaction (perspiration, tremor) is manifested.

cases. The average systolic blood pressure before the administration of insulin was 114 mm.; after insulin, 116 mm.—an increase of 1.7 per cent. The average diastolic blood pressure before insulin was 68; after insulin, 57—a diminution of 16.1 per cent. The pulse pressure became increased 29 per cent, from an average of 46 mm. of mercury before insulin to 59 mm. after insulin. Ernstene and Altschule,[15] in similar experiments, made substantially the same observations.

The pulse rate became slightly increased in four of the fourteen cases and showed no significant rise in the remaining ten cases.

15. Ernstene, A. C., and Altschule, M. D.: The effect of Insulin Hypoglycemia on the Circulation, J. Clin. Investigation **10**:521, 1931.

Effect of Epinephrine on the Insulin Reaction (table 4).—Because other investigators have stated that most, if not all, of the symptoms of the insulin reaction are due to a secondary epinephrine effect (to be discussed later), it was thought desirable to study the effect of epinephrine with the method outlined. Accordingly, a number of patients were given injections of the drug intravenously, and samples of blood from the various vessels were analyzed for dextrose and oxygen content. Despite the development of marked pallor, tremor, etc., there was but little change in the brachial-jugular or brachial-basilic differences in dextrose or oxygen. In addition, four patients were given epinephrine intravenously at the height of the insulin reaction. The brachial-jugular difference in oxygen content, which had become diminished after the administration of insulin, became more normal. The

TABLE 4.—*Effect of Epinephrine on the Blood Sugar and Oxygen*

Patient	Epinephrine, Cc.	Brachial-Jugular Difference in Dextrose Content		Brachial-Jugular Difference in Oxygen Content	
		Before	After	Before	After
A. McN.	0.2	18	12	6.33	4.90
J. P.	0.2	12	7	6.82	6.34
E. T.	0.3	7	5	6.61	....
J. B.	0.3	0	12	6.85	7.03
A. F.	0.3	16	17	6.15	6.79
M. D.	0.3	11	12	6.61	5.51
H. H.	1.0 (i.m.)	14	17	6.34	5.81
W. B.	1.0 (i.m.)	5	14	3.02	4.46
H. B.	0.5	8	8	5.29	7.39
E. B.	0.5	12	8	6.95	6.38
M. D.	0.4	14	9	6.37	4.72
L. K.	0.5	11	8	5.78	6.79

original symptoms and signs of the insulin reaction returned after the effects of epinephrine had become diminished. A protocol of a typical experiment of this type follows:

9:00 a.m.: Insulin, 60 units, given. Pupils, 3.5 mm. in diameter. Blood sugar, brachial, 92 mg. per hundred cubic centimeters; brachial-jugular difference, 7. Oxygen content, brachial, 20.1 per cent; internal jugular, 13.6 per cent; brachial-jugular difference, 6.5. Arterial blood pressure, 110 systolic and 70 diastolic; pulse rate, 96. Spinal fluid pressure, 110 mm. of spinal fluid.

9:07 a.m.: Arterial blood pressure, 110 systolic and 70 diastolic; pulse rate, 100. Spinal fluid pressure, 130 mm.

9:12 a.m.: Pupils, 3.5 mm. Arterial blood pressure, 112 systolic and 70 diastolic; pulse rate, 100. Spinal fluid pressure, 150 mm.

9:17 a.m.: Pupils, 3.5 mm. Arterial blood pressure, 110 systolic and 70 diastolic; pulse rate, 100. Spinal fluid pressure, 170 mm.

9:22 a.m.: Pupils, 3.5 mm. Arterial blood pressure, 110 systolic and 80 diastolic; pulse rate, 104. Spinal fluid pressure, 170 mm.

9:31 a. m.: Spinal fluid pressure, 120 mm.

9:32 a. m.: Arterial blood pressure, 118 systolic and 66 diastolic; pulse rate, 112. Spinal fluid pressure, from 170 to 180 mm.

9:35 a. m.: Pupils, 2.5 mm.; slight tremor; slight perspiration. Spinal fluid pressure, from 190 to 210 mm.

9:37 a. m.: Patient in distress. Arterial blood pressure, 118 systolic and 60 diastolic; pulse rate, 108. Spinal fluid pressure, from 230 to 240 mm.

9:40 a. m.: Blood sugar, brachial, 46 mg. per hundred cubic centimeters; jugular, 35 mg.; brachial-jugular difference, 11. Oxygen content, brachial, 20 per cent; internal jugular, 15.5 per cent; brachial-jugular difference, 4.5.

9:42 a. m.: Pallor; limpness of muscles; pupils, 1.5 mm. in diameter; slight tremor; marked perspiration. Arterial blood pressure, 126 systolic and 66 diastolic; pulse rate, 108. Spinal fluid pressure, from 240 to 250 mm.

9:45 a. m.: Epinephrine, 0.7 cc., given.

9:46 a. m.: Pulse irregular. Arterial blood pressure, 200 systolic and 120 diastolic. Spinal fluid pressure, 280 mm.

9:47 a. m.: Pupils, 3.5 mm.; no tremor. Arterial blood pressure, 120 systolic and 80 diastolic; pulse rate, 80. Spinal fluid, from 195 to 205 mm.

9:50 a. m.: Limpness of muscles; no tremor; marked perspiration.

9:51 a. m.: Blood sugar, brachial, 63 mg. per hundred cubic centimeters; jugular, 61 mg.; brachial-jugular difference, 2. Oxygen content, brachial, 19.9 per cent; internal jugular, 14.7 per cent; brachial-jugular difference, 5.2.

10:02 a. m.: Pupils, 3.5 mm.; no tremor; no perspiration. Blood sugar, brachial, 47 mg. per hundred cubic centimeters; jugular, 43 mg.; brachial-jugular difference, 4. Oxygen content, brachial, 20 per cent; internal jugular, 15.3 per cent; brachial-jugular difference, 4.7. Arterial blood pressure, 96 systolic and 60 diastolic; pulse rate, 92. Spinal fluid pressure, from 150 to 160 mm.

COMMENT

1. THE THEORIES FOR THE MECHANISM OF THE NEUROLOGIC SYMPTOMS OF HYPOGLYCEMIA

The Anoxemia Theory.—Much of the stimulus for this investigation was initiated by an article by Holmes.[16] In a series of experiments with the oxygen consumption of bits of brain cortex, brain white matter, spinal cord and peripheral nerve, Holmes found (1) that the gray matter of the brain took up a much greater quantity of oxygen than did white matter or peripheral nerve; (2) that the oxygen uptake of gray matter became greatly elevated when dextrose was added to Ringer's solution; (3) that the oxygen uptake of gray matter in ani-

16. Holmes, E. C.: Oxidations in Central and Peripheral Nervous Tissue, Biochem. J. **24**:914, 1930.

mals given injections of insulin was considerably less than that in the brains of normal animals; (4) that the greatly increased oxygen uptake of gray matter in the presence of dextrose was dependent on the conversion of this substance to lactic acid. These results of Holmes led us to attempt these somewhat analogous experiments on human subjects.

Olmsted and Logan,[17] in 1923, showed by decerebration and decapitation experiments on cats that the origin of the insulin convulsion was probably in the medulla, more specifically, in the respiratory center. They were the first to suggest that anoxemia is an important factor in the genesis of the convulsion: "It may possibly be that through the lowering of the blood sugar certain oxidative processes become depressed to such a degree that the brain cells, which are known to be especially susceptible to lack of oxygen, are affected in much the same manner as in asphyxia." They noted (1) the similarities between the convulsions of insulin hypoglycemia and those of asphyxia and (2) the "dark and venous character" of the arterial blood when the sugar content was very low. In later experiments Olmsted and Taylor [18] found a slight fall in oxygen saturation of the arterial blood of dogs following an insulin convulsion. Kleitman and Magnus,[19] in 1924, in experiments on rabbits, found that hypoglycemia led in some way to an irritation of the medulla and thus to convulsions. They also noted the striking similarities in the convulsions caused by insulin and by asphyxia, but disagreed with the suggestion of Olmsted and Logan that the convulsions were due to anoxemia. They noted "arterialization" of the blood. No data as to whether this applied to venous or arterial blood and no analyses of the oxygen content of the blood were reported.

Among the more constant features of the severe insulin reaction of our experiments was a definite diminution of the arteriovenous difference in oxygen content. From the experiments of Holmes [16] it appears that dextrose is essential in the normal utilization of oxygen by brain tissue. In the hypoglycemic state the uptake of oxygen by the brain (at least as measured by arteriovenous differences) appears to be materially reduced. This, together with the well known sensitivity of the brain to diminution in its oxygen supply, may account for such phenomena as tremor, twitchings and convulsions, the end-result of the lack of oxygen being coma.

17. Olmsted, J. M. D., and Logan, H. D.: The Effect of Insulin on the Central Nervous System and Its Relation to the Pituitary Body, Am. J. Physiol. **66**:437, 1923.

18. Olmsted, J. M. D., and Taylor, A. C.: The Effect of Insulin on the Blood: I. Changes in Oxygen Saturation, Percentage Hemoglobin and Oxygen Capacity, Am. J. Physiol. **69**:142, 1924.

19. Kleitman, N., and Magnus, R.: Zur Wirkung des Insulins auf das Nervensystem, Arch. f. d. ges. Physiol. **205**:148, 1924.

The Epinephrine Theory.—Much emphasis has been placed on the rôle of the sympathetic nervous system and of the suprarenal glands in the insulin reaction. Cannon, McIver and Bliss,[20] in 1924, demonstrated that excitation of the sympathetic nervous system occurred with marked hypoglycemia. The rise in rate of the denervated heart, dilatation of the pupils, tremor and the other symptoms of the insulin reaction have been ascribed to the effects of suprarenal stimulation rather than to the direct results of the hypoglycemic state (Abe,[21] Kugelman [22]).

That these symptoms are due to an increase in the epinephrine content of the blood during the hypoglycemic state has not been entirely proved. Against this assumption are the following data brought out in our experiments: (1) the diminution of the tremor and perspiration of the insulin reaction after injection of epinephrine; (2) the lack of dilatation of the pupil during the insulin reaction; (3) the striking difference between the type of effect produced by insulin and that by epinephrine on the chemical constituents of the blood.

It cannot be denied that the presence of the suprarenal glands and of an intact sympathetic nervous system are apparently necessary in combating the effects of hypoglycemia, the mechanism being one of glycogenolysis with a resultant rise in the circulating blood sugar.[23] To adduce from this, however, that most or all of the symptoms of the insulin reaction are therefore due to an increase in the circulating epinephrine seems somewhat unwarranted.

The Theory of Disturbed Water Balance.—Olmsted and Taylor [18] concluded from studies of the oxygen capacity of the blood that the blood became concentrated when the blood sugar reached its lowest level. Rathery and Sigwald,[24] studying insulin hypoglycemia in dogs, found a constant elevation of the plasma chlorides and a decrease in the spinal fluid pressure. On the other hand, Drabkin and Ravdin [25] found that the cerebrospinal fluid pressure of dogs rose with the fall in blood sugar. On the basis of these and previous experiments (Drabkin and

20. Cannon, W. B.; McIver, M. A., and Bliss, S. W.: Studies on the Conditions of Activity in Endocrine Glands: XIII. A Sympathetic and Adrenal Mechanism for Mobilizing Sugar in Hypoglycemia, Am. J. Physiol. **69**:46 (June) 1924.

21. Abe, Y.: Das Verhalten der Adrenalinsekretion bei der Insulinvergiftung, Arch. f. exper. Path. u. Pharmakol. **103**:73, 1924.

22. Kugelman, B.: Ueber die Beziehungen zwischen Insulin und Adrenalin im menschlichem Organismus, Klin. Wchnschr. **10**:59, 1931.

23. Dworkin, Simon: The Response of Sympathectomized Animals to Insulin, Am. J. Physiol. **98**:467, 1931.

24. Rathery, F., and Sigwald, J.: Etude expérimentale des modifications humorales dans l'hypoglycémie insulinique chez le chien, Compt. rend. Soc. de biol. **107**:1074, 1931.

25. Drabkin, D. L., and Ravdin, I. S.: Mechanism of Convulsions in Insulin Hypoglycemia, J. Biol. Chem. **157**:3, 1930.

Shilkret [26]) they concluded that insulin convulsions were caused by an increased cerebrospinal fluid pressure resulting from anhydremia. It is conceivable that the edema of the brain described by Schereschewsky, Mogilnitzky and Gorjaewa [27] in animals and by Bowen and Beck [1b] in a human case might be secondary to a disturbance in oxidative mechanisms in the brain and not a primary manifestation. Bowen and Beck [1b] found extreme edema of the brain and spinal cord and a very small amount of spinal fluid at necropsy in a fatal case of insulin hypoglycemia. They suggested, therefore, that the cerebral symptoms of the hypoglycemia reaction were caused by or related to the hydration of the central nervous system which may have occurred with anhydremia of the circulation.

No increase in oxygen capacity was noted in our experiments. Frequent red blood cell counts in a group of patients after the administration of insulin failed to show any change.

2. LACTIC ACID AND DEXTROSE

As already noted, there was a constant increase in the circulating lactic acid during the height of the insulin reaction, due probably, as noted by other investigators,[28] to the increased activity of muscles (tremor) at the height of the reaction. There was essentially no difference, however, in concentration of lactic acid between the samples of blood removed from the various vessels. It could not be determined from our experiments whether the conversion of lactic acid from dextrose was diminished in the brain during hypoglycemia.

The striking contrast in the behavior of the arteriovenous differences in dextrose content between the brain and the arm has already been noted. This is possibly explained by the increased utilization of dextrose by muscle in the presence of insulin hypoglycemia, as noted by several previous investigators.[29]

3. VALIDITY OF EXPERIMENTS

The conclusions drawn from our experiments depend on differences in the content of dextrose and oxygen in blood from different vessels before and after the administration of insulin. It is realized that obser-

26. Drabkin, D. L., and Shilkret, H.: Insulin Anhydremia; Importance of Water Reserve in Physiological Crisis, Am. J. Physiol. **83**:141, 1927.

27. Schereschewsky, N. A.; Mogilnitzky, B.N., and Gorjaewa, A. W.: Zur Pathologie und pathologischen Anatomie der Insulinvergiftung, Endokrinologie **5**:204, 1929.

28. Best, C. H., and Ridout, J. H.: Observations on Blood Lactic Acid After Insulin, J. Biol. Chem. **63**:197, 1925.

29. Cori, C. F.; Cori, G. T., and Goltz, H. L.: Comparative Study of the Blood Sugar Concentration in the Liver Vein, the Leg Artery and the Leg Vein During Insulin Action, J. Pharmacol. & Exper. Therap. **22**:355 (Dec.) 1923.

vations in which the actual consumption of metabolites by various tissues is not directly measured may be subject to error. Particularly is this true when the differences between artery and vein are taken as representing the usage of a given substance by an organ. The experiments cited do not take into account three important factors, namely: (1) the volume of the brain as compared with the volume of the arm; (2) possible changes in the blood flow through the brain and the arm as accounting for the changes noted in the chemical constituents of the blood; (3) possible differences in distribution of metabolites before and during the insulin reaction.

The first factor could not be measured, although approximate measurements might have been made. Since, however, the experiments dealt with the same organs before and after the administration of insulin, this factor was not considered important. It is conceded that changes in the rate of blood flow through the arm and the brain may have affected our results. Weiss and Lennox [30] in experiments with histamine, which probably increases the blood flow through the brain, stated that the difference in oxygen content between an artery and the internal jugular vein decreases during the administration of histamine. In three experiments of our own in which histamine was used, no change in the brachial-jugular differences in dextrose or oxygen content developed. Again, epinephrine has been shown to increase the velocity of the blood flow.[31] Our experiments with this drug, however, failed to show any material change in oxygen uptake by the brain as measured by the difference in oxygen content of an artery and the internal jugular vein. Possible changes in the distribution of metabolites before and after the injection of insulin might conceivably have influenced our results. These were, however, so consistent as to invalidate that possibility. The difference in behavior of dextrose between the brain and the forearm after the injection of insulin may be said to speak for difference in the metabolism of these organs as determined by arteriovenous differences.

SUMMARY AND CONCLUSIONS

1. An attempt was made to study the mechanism of the neurologic symptoms of insulin hypoglycemia in man, chiefly by comparing the contents of dextrose and oxygen in the vessels supplying the brain and the arm before and after the intravenous administration of insulin.

2. Samples of blood were obtained as nearly simultaneously as possible from the brachial artery, the internal jugular vein and (usually)

30. Weiss, S., and Lennox, W. G.: The Cerebral Circulation: XVII. Cerebral Blood Flow and the Vasomotor Response of the Minute Vessels of the Human Brain to Histamine, Arch. Neurol. & Psychiat. **26**:737 (Oct.) 1931.

31. Blumgart, H. L.: The Velocity of Blood Flow in Health and Disease: VII. The Effect of Epinephrine on the Velocity of Blood Flow, Medicine **10**:36, 1931.

a basilic vein; they were analyzed for content of dextrose, oxygen, carbon dioxide and (frequently) lactic acid. Usually the arterial blood pressure, the spinal fluid pressure (and dextrose content), the pulse rate and the associated symptoms of the hypoglycemic reaction were studied.

3. The following results were obtained: (*a*) The chemical changes in the blood usually varied directly with the severity of the reaction.

(*b*) The uptake of dextrose by the brain (as measured by the difference in dextrose content of an artery and the internal jugular vein) became materially reduced during the severe hypoglycemic reaction, although that of the arm usually became increased.

(*c*) The uptake of oxygen by the brain (as determined by arteriovenous differences in oxygen content) varied indirectly with the severity of the insulin reaction, becoming much reduced during the most severe reactions.

(*d*) The blood lactic acid became increased during the reaction, no differences between vessels being noted.

(*e*) The spinal fluid pressure regularly became increased before the objective phenomena of the hypoglycemic reaction could be seen. There was no essential change in the dextrose content of the spinal fluid during the period of observation (from forty-five to ninety minutes).

(*f*) The pulse pressure usually became increased, owing to a slight rise in systolic pressure and to a more marked fall in diastolic pressure.

4. The effect of superimposing an injection of epinephrine on the insulin reaction was studied. Epinephrine regularly diminished the symptoms of the insulin reaction.

5. Various theories explaining the neurologic symptoms of the hypoglycemic reaction are discussed, and the epinephrine theory is critically analyzed.

6. The marked diminution in the arteriovenous difference in content of oxygen during the severe insulin reaction may signify actual diminution in oxygen uptake by the brain and arm. If this is true, the neurologic symptoms of the insulin reaction may be due to the effects of a lack of oxygen on brain tissue.

TREATMENT FOR THE PRIMARY MYOPATHIES

HANS H. REESE, M.D.

E. MURRAY BURNS, M.D.

AND

CAROL M. RICE, M.D.

MADISON, WIS.

The concept of the primary myopathies is, as yet, not firmly established, and the characteristics of the various groups of muscular dystrophies are not universally delineated. The many etiologic factors have been debated but have remained obscure and, therefore, no rational therapy can be advocated. The contractile processes in the muscles, whether they are of metabolic or of neurogenic nature, have kept physiologists and biochemists busy, and the investigations have resulted finally in the Hill-Meyerhof formulation, which, unfortunately, does not explain the problem of muscular fatigue.

The differential diagnosis between primary and secondary myopathies is clinically difficult and, we believe, at times impossible without the estimation of creatine and creatinine. Whereas the primary myopathies are accompanied by alterations in the metabolic creatine, the secondary myopathies are not associated with such changes. Important points in the differential diagnosis are heredity, age, electrical reactions, pathologic changes observed at biopsies of muscles, and the progress of muscular involvement with or without pseudohypertrophies, but these points alone are insufficient for accurate diagnosis.

Differences in the forms and conditions of dystrophic muscles are noticeable by inspection and palpation. The histologic observations often reveal a mixture of hypertrophic, abnormally developed (pseudohypertrophic?) and atrophic muscle fibers with proliferation of connective tissues and various degrees of fatty degeneration and of reduction in nuclear proliferation. Pseudohypertrophies may occur only in the late stages of the primary myopathies when the contractility of the muscles has decreased to practical dysfunction. Schultze,[1] in a monograph, referred to a case of secondary myopathy in which such hypertrophic, pseudohypertrophic and atrophic muscle fibers with fatty degenerations were present.

From the University of Wisconsin Medical School.

Read at the Meeting of the Chicago Neurological Society, Dec. 21, 1933.

1. Schultze, F.: Ueber den mit Hypertrophie verbundenen progressiven Muskelschwund und ähnliche Krankheitsformen, Wiesbaden, F. Schultze, 1886.

We do not believe that the hypertrophic fibers are the result of replacement hypertrophy or that they are conditioned by better regional nutrition. It is known that muscle fibers may increase in size (not swelling) following pressure from a tumor or as a result of other irritations, but in such conditions the striation is preserved without the alterations seen in primary myopathies. The presence of striation in affected muscles does not permit clinical deductions, as striation remains intact for a long time in the course of spinal diseases, such as amyotrophic lateral sclerosis and poliomyelitis, and in cases of polyneuritis. Hypertrophies or pseudohypertrophies of muscles in neuritic atrophies have been described only once in the literature.

An interesting question in this problem of primary myopathies centers around the nerve end-plates and their attachment to and detachment from the muscle fibers. We cannot make clear deductions from the histologic reports in the literature pertaining to this question.

The statements that the muscular dystrophies are conditioned by dysfunctions in the endocrine ring or in the sympathetic system are worthy of consideration. In our experience, endocrine dysfunctions in the primary myopathies are so slight, as measured from our studies on metabolism and biochemistry, that they can in most cases be disregarded.[2]

Ken Kuré and S. Okinaka's therapy with pharmacologic stimulants, such as pilocarpine and epinephrine, has not found many followers. We have treated patients with these drugs, giving 0.2 cc. of 1 : 1,000 solution of epinephrine (ephedrine is not effective) with 0.1 cc. of a 1 per cent solution of pilocarpine by daily injections for one week and then every second and third day. If we did not get sufficient reaction from this mixed injection we increased the dose. All the patients complained of palpitation of the heart, paresthesias and tension in the affected muscles, and became slightly excited for from two to three hours. We have not continued these injections, but from the literature we know that after such a period of medication the results decrease, and that on omission of the drugs the muscular fatigue and associated disabilities become definitely increased. We know of one case in which 110 injections were given with an initial improvement, but after the seventieth injection there was a lack of stimulation and on cessation of injections a complete collapse. This patient improved greatly thereafter under medication with glycine.

2. These studies will be reported in detail in the Journal of Nervous and Mental Disease.

Increased knowledge of the production of creatine has offered clinical medicine a new rational therapy for muscular disorders. It has been observed that small amounts of creatine ingested are retained by normal persons, whereas patients with true myopathies excrete the ingested creatine almost in the total amount. It has also been noticed that in such patients creatine is excreted even on a creatine-free diet. In attempting to determine the rôle of amino-acids in the production of creatine, Brand, Harris, Sandberg and Ringer [3] administered glycine to patients with muscular dystrophy and obtained an increased output of creatine in the urine.

Milhorat, Techner and Thomas [4] recognized that a prolonged administration of glycine may influence the course of muscular dystrophy. Accordingly they fed glycine in daily doses of from 5 to 20 Gm. and observed a variable increase in the output of creatine for from two to eight weeks and then a return to the former limits. Also, it was found that as the output of creatine decreased, that of creatinine increased. This indicated that as creatine is stored, the end-product of its metabolism (creatinine) is excreted in its place (we shall refer again to this point later). Milhorat and his co-workers observed subjective improvement coincident with the storage of creatine, which continued as long as glycine was administered. They concluded that glycine has an important function in the physiology of the muscles and a significant rôle in the pathogenesis of myopathic diseases, as well as in the treatment for these diseases. Regarding the therapeutic value of glycine, however, the more recent observations of Harris and Brand [5] are less encouraging. On the other hand, clinical investigations in general seem to indicate some value from the use of glycine. In addition to the aforementioned data, the investigation of Kostakow and Slauck, Mettel and Slocum, Reinhold and his associates and Beard and Tripoli have been quite encouraging. The results obtained by Boothby and (separately) by Remen with similar therapy in myasthenia gravis also appear hopeful. The work of Chanutin, Butt and Royster, while incomplete, is also encouraging.

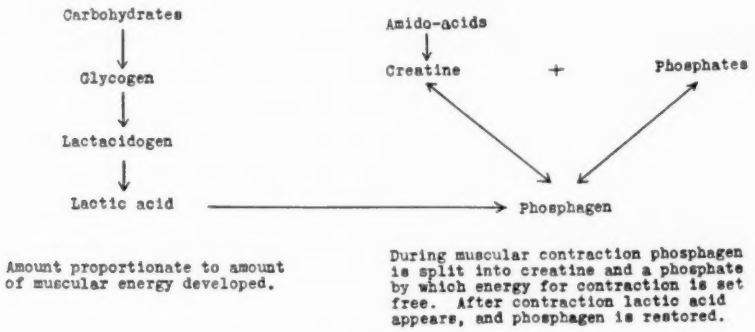
In an attempt to explain the rôle of glycine we are led to a review of the newer concepts of the physiologic processes in the muscles.

3. Brand, E.; Harris, M. M.; Sandberg, M., and Ringer, A. L.: Am. J. Physiol. **90**:296, 1929.

4. Milhorat, A. T.; Techner, F., and Thomas, K.: Ztschr. f. physiol. Chem. **205**:93, 1932; Proc. Soc. Exper. Biol. & Med. **29**:609 (Feb.) 1932.

5. Harris, M. M., and Brand, E.: J. A. M. A. **101**:1047 (Sept. 30) 1933.

On the basis of the work of P. Eggleton and G. P. Eggleton and of Lundsgaard, as epitomized by Hill,[6] we may postulate the following mechanism:


Carbohydrates
Glycogen
Lactacidogen
Lactic acid
Amido-acids
Creatine
+
Phosphates
Phosphagen
Amount proportionate to amount of muscular energy developed.
During muscular contraction phosphagen is split into creatine and a phosphate by which energy for contraction is set free. After contraction lactic acid appears, and phosphagen is restored.

From the diagram it will be noted that during muscular contraction phosphagen or phosphocreatine (a labile compound of creatine and an organic or an inorganic phosphate) is broken down into its two main components, as illustrated in the diagram. This reaction is exothermic and supplies the energy for muscular contraction. After contraction lactic acid accumulates from the breakdown of glycogen. In the presence of oxygen and lactic acid phosphagen is resynthesized (a portion is resynthesized in the presence of oxygen alone without lactic acid and constitutes an exothermic aerobic recovery; the anaerobic recovery of phosphagen—due to lactic acid without oxygen—is endothermic). If the formation of lactic acid is retarded (as in an experiment performed by Smith and Visscher[7] with iodo-acetic acid poisoning), the resynthesis of phosphagen is disturbed. However, the muscle may contract without lactic acid so long as phosphagen is still present and partially resynthesized by oxygen. Four fifths of the lactic acid is reconverted into glycogen. The energy for contraction, then, is produced by the breakdown of phosphagen, while the production of lactic acid offers the energy for the resynthesis of phosphagen.

It is the production of creatine in this mechanism that offers the greatest source of speculation. From all available evidence it appears that creatine is formed either from or by amino-acids.[8] The stimu-

6. Hill, A. V.: The Revolution in Muscle Physiology, Physiol. Rev. **12**:56 (Jan.) 1932.

7. Smith, P. W., and Visscher, M. B.: Am. J. Physiol. **102**:448, 1932.

8. Beard, H. H., and Barnes, B. O.: The Influence of Feeding Proteins, Amino-Acids, and Related Substances upon Creatine-Creatinine Metabolism, J. Biol. Chem. **94**:49 (Nov.) 1931. Beard, H. H.: Influence of Protein and Amino-Acid Feeding upon Creatine Formation, and Creatinine Elimination in Urine, Proc. Soc. Exper. Biol. & Med. **28**:454, 1931.

lation of metabolic activity by amino-acids suggests a specific dynamic action, but this does not appear to be associated with the formation of creatine, for certain amino-acids which give the best production of heat give less increase in muscular creatine. Brand and Harris recently pointed out that the administration of benzoic acid in muscular dystrophy resulted in a decrease in the output of creatine.[9] Assuming that the muscular creatine is not increased thereby, and considering that benzoic acid unites with available glycine to form hippuric acid, it appears that the formation of creatine depends (in part, at least) on the storage of glycine. On the basis of the excretion of hippuric acid, Freiberg and West [10] found that in three patients with well advanced pseudohypertrophic muscular dystrophy glycine was produced (i. e., hippuric acid was excreted) in response to benzoic acid in the same manner as in normal controls. Glycine, therefore, is probably available but either is not utilized or is not stored in the dystrophic muscles.

If this is the case (the formation of creatine is dependent on the storage of glycine) it is probable that muscular contraction is disturbed because of a secondary depletion of creatine and consequently of phosphagen in the muscle.

In this connection it is of interest to note that Goettsch and Brown [11] produced nutritional muscular dystrophy in rabbits and found a decrease of creatine in the skeletal muscles to a level normal for the myocardium but not for the visceral muscles. They concluded that creatine is probably bound in more than one way in striated muscle (possibly with phosphocreatine), and that a decreased creatine content of muscle indicates muscular atrophy, but is only a rough index to its severity.

Closely related to this picture is the muscular asthenia of exophthalmic goiter. Shorr, Richardson and Wolff [12] recently demonstrated that this type of weakness may be an "acute muscular dystrophy," because the findings concerning creatinuria with and without glycine closely simulate those obtained in muscular dystrophy. Glycine is available in exophthalmic goiter, as is shown by the fact that the output of hippuric acid is normal in response to feeding with benzoic acid. They believed that the disturbance in exophthalmic goiter lies in the mechanism of the lability of phosphocreatine rather than in storage of glycine.

We have stressed the theory of creatine depletion secondary to nonutilized glycine in the dystrophic muscle as being responsible for the disturbed physiologic process. Another explanation lies in assuming

9. Brand, Harris, Sandberg and Ringer.[3] Harris and Brand.[5]

10. Freiberg, I. H., and West, E. S.: Glycine Synthesis in Pseudohypertrophic Muscular Dystrophy, J. Biol. Chem. **101**:449 (July) 1933.

11. Goettsch, M., and Brown, E. F.: J. Biol. Chem. **97**:549, 1932.

12. Shorr, E.; Richardson, H. B., and Wolff, H. G.: The Nature of Muscular Weakness in Graves' Disease, J. Clin. Investigation **12**:966 (Sept.) 1933.

a hypometabolic activity in the dystrophic muscle, which is accelerated by excess ingestion of amino-acid.

We turn now to the therapy. Glycine is given in amounts of from 5 to 20 Gm. daily in divided doses, the amount depending on the degree of creatinuria. We have also given glutamic acid in daily doses of 10 Gm.[13] Both amino-acids are given orally. Glutamic acid, because of its rather disagreeable taste, bears sweetening. Beard [14] demonstrated that creatine is of exogenous as well as of endogenous source, and for this reason purines had best be supplied in the diet. It is to be remembered that there is a long latent period in clinical response, and that the administration of amino-acid must be continued throughout this time.

The effect of therapy during this latent period must be followed by studies on creatine in twenty four-hour specimens of urine. For exact determinations a weighed diet is necessary, but for outpatients such a procedure is impracticable. We have found that an irregular but satisfactory curve for the excretion of creatine is obtained with a general diet. Determinations can be made once a week. Even though it is impracticable, an accurate twenty-four hour measurement must be obtained, otherwise results vary widely, and no conclusions can be drawn. Both creatine and creatinine should be estimated.

Kostakow and Slauck [15] demonstrated a definite rise in creatinuria after from two to five days, the peak varying for different subjects at from two to eight weeks, then returning to the initial level and eventually to the normal. As the level for creatine drops, that for creatinine rises. This is explained on the basis that creatinine is the excretory product of the normal metabolism of creatine; in the dystrophies creatine is not stored and is excreted as such. When, under treatment, creatine begins to be stored, the metabolism of creatine returns to normal and the excretory product of this metabolism is given off in place of the now utilized creatine. It seems, then, that the drop in the level of creatine and the rise in that of creatinine is the laboratory indication of a response to therapy. Repeated glycine therapy reveals a slower response of creatine, but this remains longer in the normal range. The administration of glycine may be discontinued while the normal level of creatinuria persists, but glycine should be administered again when the level of creatinine drops (or that of creatine rises).

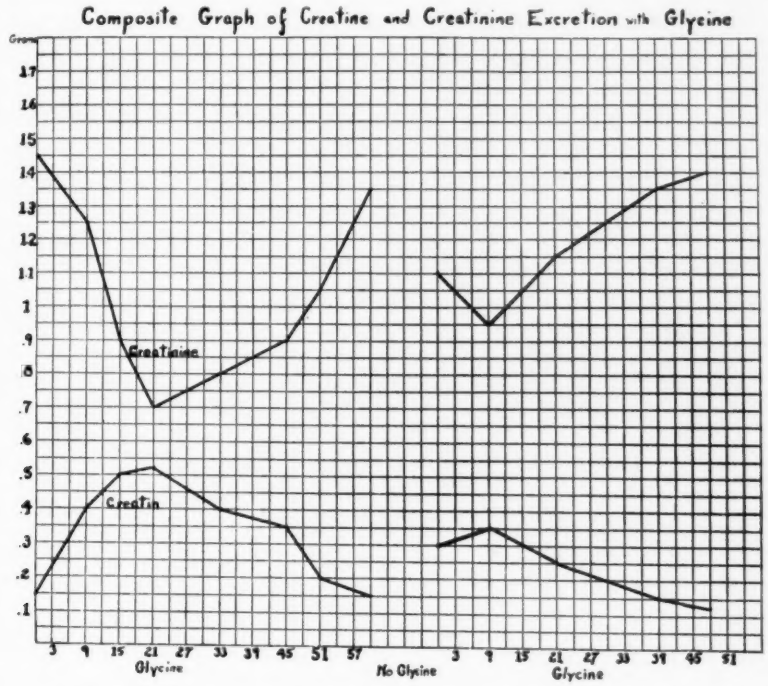
13. H. H. Beard furnished information regarding the use of glutamic acid in our investigation.

14. Beard, H. H.: A Biometric Study of the Relation Between the Excretion of Creatinine Nitrogen and Several Body Measurements, Human Biol. **4**:351 (Sept.) 1932.

15. Kostakow, H., and Slauck, A.: Die Glycokollbehandlung der progressiven Muskeldystrophie, Deutsche med. Wchnschr. **5**:169, 1933.

The chart presents a composite graph of the mean values of creatine and creatinine excretion; the actual values determined are quite variable (note the similarity of the chart to the graph recorded by Kostakow and Slauck[15]). As was pointed out by Adams,[16] the increase in creatine appears to be influenced by the degree of the creatinuria before the administration of glycine.

Occasionally clinical response is first noticed in muscular paresthesias and vague muscular pains. Improvement manifests itself first by a decrease in fatigability and malaise associated with mental alertness.



Composite graph of creatine and creatinine excretion with glycine.

Next there is an increase in muscular strength, and finally an increase in muscular weight. It appears that glutamic acid causes more muscular paresthesias than does glycine.

Reinhold[17] and his associates recently studied muscle tissue before and after treatment with glycine. They reported that specimens of muscle revealed improvement in chemical and histologic structure.

16. Adams, M.: Metabolism Studies Following the Administration of Glycine, unpublished data.

17. Reinhold, J. G.; Clark, J. H.; Kingsley, G. R.; Custer, R. P., and McConnell, J. W.: The Effects of Glycine (Glycocoll) in Muscular Dystrophy, J. A. M. A. **102**:261 (Jan. 27) 1934.

REPORT OF CASES

CASE 1.—*History.*—F. M., a white boy, aged 10, did not walk until 2¼ years of age and never ran like other children. He stumbled and fell frequently. In the past few years he had been unable to climb the stairs. His brothers took him to school on a bicycle. His school work had always been good.

Physical Examination.—There were: a waddling gait, lordosis, winged scapulae, marked wasting of the muscles of the shoulder and pelvic girdles and enlargement of calf muscles, although the latter were weak as were all the groups. The patient was unable to come to a sitting position without first rolling over. He presented the typical "climbing up" method of assuming the upright position. Areflexia was present.

Laboratory Studies.—Biopsy of a calf muscle showed changes typical of pseudohypertrophy.

Diagnosis.—A diagnosis of pseudohypertrophic muscular dystrophy was made.

Course.—Six grams of glycine was administered daily for nine months. There was a slight subjective improvement. No paresthesias occurred.

CASE 2.—J. E., a white boy, aged 8, had had a normal infancy and walked at 18 months, but at the age of 3 years the family noticed that the gait was unusual. He had a hollow back, was unsteady and fell often. There had been a progression of symptoms, and gradually it became necessary for him to roll over and push up to come to a sitting position, and to "climb up" the thighs in order to stand.

Physical Examination.—The outstanding points were underdevelopment and wasting of the muscles with marked enlargement of the calf, deltoid and masseter muscles. He had to "climb up"; he walked with a wide base, marked lordosis and a waddling gait.

Laboratory Studies.—No biopsy was made.

Diagnosis.—There was pseudohypertrophic muscular dystrophy.

Course.—Glycine, 10 Gm., was administered daily for three months. A teacher reported that whereas it had been necessary to lift the child from the floor from four to five times a day, it was now not necessary to do so more than from four to five times a week. No paresthesias were present.

CASE 3.—H. A., a white housewife, aged 46, had experienced the onset of generalized weakness at the age of 31. Pregnancies that had occurred since had been normal, and delivery had not been unduly prolonged. Periods of rest had been necessary during any activity, even during meals. Diplopia occurred with fatigue.

Physical Examination.—There were: generalized weakness, easy fatigability and a myasthenic reaction.

Laboratory Studies.—The Jolly reaction was present. The results of biopsy were not typical.

Diagnosis.—A diagnosis of myasthenia gravis was made.

Course.—Ephedrine was given first, with relief; glycine was then given alone, with relief; the two drugs were then administered together, with the most relief. The duration of the combined treatment was nine months.

Course.—No paresthesias occurred. The condition was much improved and the patient became able to do all of her housework. There was no diplopia.

CASE 4.—P. T., a white man, aged 56, had experienced the onset of ptosis of the right upper lid five months before admission. On one occasion he had been unable to sing because of fatigue.

Physical Examination.—There were: ptosis, more marked on the right than on the left, paresis of upward gaze, weakness of the right orbicularis oculi and frontalis, high myopia and hypertension.

Laboratory Studies.—No biopsy was performed.

Diagnosis.—A diagnosis of myasthenia gravis was made.

Course.—Glycine was given alone because of the hypertension. Subjective and objective improvement appeared after about six weeks of treatment.

CASE 5.—C. C., a white man, aged 23, at 11 years of age had noticed that he was easily fatigued and that he could not keep up with others on a hunting trip. This condition progressed until at the time when the patient was seen (twelve years after the onset) he was severely handicapped by fatigue and weakness and had a peculiar gait.

Physical Examination.—The findings were typical of a muscular dystrophy of the shoulder and pelvic girdle type. The calves were greatly enlarged.

Laboratory Studies.—A biopsy showed myomesial degeneration. There was no reaction of degeneration.

Diagnosis.—A diagnosis of pseudohypertrophic muscular dystrophy was made.

Course.—Glycine or glutamic acid, 10 Gm., was given daily for sixteen months, with two one-month periods without treatment. There were no paresthesias. The patient said that he was less easily fatigued but that weakness still persisted. He felt "much better now than before treatment, but no better now than six months ago." Apparently the condition in this patient had reached a plateau.

CASE 6.—G. C. a white man, aged 18, a brother of C. C. (case 5), with a history and findings practically identical with those of the brother, had experienced the onset at 11 years of age.

Laboratory Studies.—A biopsy showed changes identical with those in case 5. There was no reaction of degeneration.

Diagnosis.—Pseudohypertrophic muscular dystrophy was diagnosed.

Course.—Glycine or glutamic acid, 10 Gm., was administered daily for the same period and with practically the same results as in case 5.

CASE 7.—E. T., a school girl, aged 21, had noticed at the age of 16 that she easily became fatigued. Within a year the disability due to weakness and fatigue was marked. She had been unable to complete her school work.

Physical Examination.—There was marked atrophy of the scapulopelvic muscles with some enlargement of the muscles of the calf and forearm. Easy fatigability was evident.

Laboratory Studies.—No biopsy was performed.

Diagnosis.—The diagnosis was scapulopelvic muscular dystrophy.

Course.—Glycine, 10 Gm., was given daily for three months, at the end of which the patient was able to be up and to take part in the easier tasks of housekeeping.

CASE 8.—M. T., a high school girl, aged 16, a sister of E. T. (case 7), had noticed the onset of weakness and fatigue of the hip muscles particularly at 13 years of age. The remainder of her history and the findings were practically the same as in case 7.

In cases 7 and 8 the fatigue, the muscular weakness and the static functions improved steadily during the three months of glycine therapy. The patient described in case 7 is now able to work as a clerk in a drug store for hours; the patient described in case 8 is capable of walking to school (three fourths of a mile), and with the subsidence of the physical fatigue her work in school has become easier and her grades are higher. In these two cases glutamic acid produced annoying paresthesias (severe in case 8), which were not present in either case following medication with glycine.

CASE 9.—G. M., a white school girl, aged 19, had experienced the onset of marked fatigue in 1931, at the age of 17. During the following two years there were a few remissions. Treatment had consisted of tonsillectomy and thyroidectomy, both without improvement.

Physical Examination.—There were: a pseudoptosis, a myasthenic reaction in the hands and eyelids, and generalized asthenia.

Diagnosis.—A diagnosis of myasthenia gravis was made.

Course.—Glycine, 10 Gm., with ephedrine, 25 mg., was administered twice daily for three months. One definite exacerbation occurred, but in general the patient felt much better than before the medication. Charts for the dynamics of the muscles showed no improvement, however. There were no paresthesias.

SUMMARY

Therapy by endocrine and pharmacologic stimulation has proved unsatisfactory in the myopathies. Therapy with glycine or glutamic acid is encouraging and beneficial; it is recommended as the best treatment available. Clinical and biochemical investigations seem to indicate that amino-acid therapy is effective. Cures are not obtained, but definite clinical remissions as to muscular function and creatine metabolism are brought about.

DISCUSSION

DR. BENJAMIN BOSHES: My associates and I have thoroughly studied six cases of muscular dystrophy for two years. We were impressed with the reports that the creatine content decreases and subsequently increases, but there have been no statements of a subsequent increase in creatinine, except by Milhorat, Technor and Thomas (1932) and by Kostakon and Slanck (1933). The latter reported that the nitrogen metabolism approaches normal. The clinical reports have referred to muscular paresthesias, etc. Dr. Weil and I decided to measure the muscle activity by a spring scale dynamometer, and we have measured all the muscular groups in five cases of muscular dystrophy. Two of the cases were markedly advanced; two moderately advanced, and one was of the obese, hypertrophic type. We gave the children glycine, 5 Gm. daily. In the two advanced cases, in which the atrophy was marked, in two or three months the activity was not measurable. The patients with moderately advanced dystrophy responded well to glycine, and now, after about two years, they have not only held the level but have increased in strength. Whether this is due to the glycine, we are unable to state; we have had too few cases to establish controls.

In the fifth the patient has shown increased strength as measured by the dynamometer, although he cannot walk. He could walk formerly. By studying the charts we found that the gain has been in the arms, whereas the loss has been

in the legs. Concomitant with that, we noted a gain in weight of 26 pounds (11.8 Kg.). The gain in muscular strength was not equal to the gain in weight; because the boy was heavier, he was unable to walk.

In the sixth case we started therapy three months ago, and the patient has practically doubled his muscular strength.

The fact that muscular dystrophy is a progressive disease and that in these six cases three patients have become stronger make the study of the effect of glycine interesting.

We studied two cases of myasthenia gravis, in which ephedrine and glycine were used and in which glycine alone was used. Both showed an excellent response. We found that a good way to make a check of the change was by pictures of the patient, i. e., by taking pictures at the onset of the ephedrine or glycine medication and at intervals thereafter. This shows the general progress well, while the dynamometer shows the changes in muscular strength.

Have Dr. Reese and Dr. Burns used glutathione as suggested by Harris and Brand?

DR. CHARLES F. READ: What precautions have been taken to avoid the possible effect of suggestion in these cases? It is not certain that a person may not show greater strength, even with the dynamometer, under suggestion. Did these patients know when the medication was being changed?

DR. GEORGE W. HALL: What type of myopathy was treated?

DR. PERCIVAL BAILEY: I feel certain that the secret of many psychopathic as well as neurologic diseases will be discovered in the chemical laboratory; work along this line will some day reveal the nature of many disorders the existence of which is now questioned.

DR. HANS H. REESE: The two pairs of patients who are under treatment have responded well and are greatly improved. The muscle strength has been checked by dynamometric methods measuring the muscular powers of the toes and feet and of the fingers, hands and arms. The two male subjects (aged 23 and 19) were unable to walk any distance on admission, but after two courses of glycine medication reported that they were better and able to go hunting all day. As to the two sisters (21 and 16 years of age), suffering also from pseudohypertrophic myopathy, the younger is able to walk to and from school now, whereas formerly she had to be brought to school. She can now walk a mile without being fatigued. In addition to the muscular improvement, a general physical improvement has been noticed as well as an increased intellectual alertness, the latter being measured in efficiency and marks in school.

These statements are not our impressions but reports by the patients. I believe that the possibility of any psychic factor can be ruled out, because we did not obtain such definite improvement with other medications. In the beginning of this clinical study the improvement was less definite because of the small amounts of glycine given. Instead of 5 Gm. we give now daily from 10 to 15 Gm. of glycine, or 10 Gm. of glutamic acid. The therapy is a rational one. Time and more experience will reveal whether clinical arrest with a normal creatine-creatinine metabolism can be maintained.

DR. E. MURRAY BURNS: We have not used glutathione in our work. The dose of glutamic acid is about 10 Gm. daily, given in the morning. As Dr. Reese said, we get the best response in the pseudohypertrophic cases, but we get some response in both types. It has been noticed that there is some increase in muscle mass, but we cannot be sure whether it is actual hypertrophy of the muscle tissue or pseudohypertrophy.

VASOMOTOR CHANGES ASSOCIATED WITH PARALYSIS OF CEREBRAL ORIGIN

PAUL C. BUCY, M.D.
CHICAGO

Vasomotor changes in extremities paralyzed by cerebral lesions have long been recognized. There has, however, been considerable question as to the correct interpretation of the manifestations which have been observed. A review of the extensive literature dealing with the recorded cases will be presented later. In the case reported here, the vasomotor changes, observed from the onset of the paralysis, were far more marked and definite than those usually reported. Because of the unequivocal character of these changes their relation to the known physiologic activity of the central and peripheral portions of the sympathetic nervous system seems clear. The case is presented in order to facilitate the correlation of the physiology of the human nervous system with recent developments in the study of the cortical representation of this system in infra-human primates (Fulton, Kennard and Watts) and to stimulate additional observations of vasomotor changes early in cases of paralysis of cerebral origin, as it appears that they are most marked at that time.

REPORT OF CASE

Automobile accident resulting in temporary unconsciousness and laceration of ligaments of right knee; surgical repair of ligaments; eight days later sudden hemiplegia of right side with abolition of pulse and blood pressure on right side; rapid recovery.

R. H., a housewife, aged 45, was admitted to the University of Chicago Clinics on June 13, 1932, shortly after having been knocked down by an automobile. On admission she was unconscious, but in a few minutes she could be aroused and was soon able to give her name and address. Examination revealed lacerations of the scalp and of various extremities and a lateral dislocation of the right knee. The blood pressure on admission was recorded as 145 systolic and 85 diastolic with a mercury sphygmomanometer. Apart from the injuries just noted there were no other deviations from the normal. The lungs were clear; the heart was of normal size, and the cardiac rate and rhythm were normal. Palpation of the abdomen revealed nothing unusual. Within the limits of her injuries muscular strength was good; there were no disturbances of sensation and all reflexes were normal.

The family history revealed nothing relevant. The patient had had no previous complaints bearing on the present condition. There was no history suggestive of any cardiac, respiratory, gastro-intestinal or nervous disease.

Presented before the Harvey Cushing Society, St. Louis, April 5, 1934.

From the Division of Neurology and Neurosurgery of the University of Chicago.

Roentgenologic Examination.—Roentgenograms revealed no evidence of a fracture of the skull, right femur, elbow, wrist or foot. There was a gross separation of the femoral condyles from the articular surface of the tibia on the right, and there was an impacted fracture of the head of the right fibula.

Operation.—A diagnosis of "torn crucial and internal lateral ligaments of the right knee" was made, and on June 22, 1932, the patient was operated on and these ligaments were repaired. A plaster of paris cast including the pelvis and the entire right lower extremity except the toes was applied.

Cerebral Accident—Disappearance of Pulse on Hemiplegic Side.—On June 26 a small decubitus appeared in the gluteal fold; otherwise the postoperative course was satisfactory and uneventful until 4:30 p. m. on June 30. At that time the nurses were turning the patient in bed. She talked during the first part of this procedure, but just as it was being completed, she suddenly ceased talking; respiration became very labored, and the patient lapsed into deep coma. I saw her within a few minutes after this sudden change. She could not be aroused. Breathing was stertorous. The lips were cyanotic. There was an obvious weakness of the right side of the face. The right arm was cold and cyanotic. There was a slight cyanosis of the left upper extremity, but it was distinctly warm. The pulse was unobtainable in the right radial artery.

At 5 p. m., about one-half hour after the onset, the patient began to moan and roll her head from side to side. The pupils were equal; both reacted to light. The ocular fundi and disks were perfectly normal. The right arm at this time was completely flaccid, very cold and cyanotic, and the pulse was barely perceptible at the wrist. Painful stimuli applied to the right upper extremity elicited no evidence of perception, whereas similar stimulation on the left side invariably evoked movement and evidence of displeasure. The left upper extremity was warm and no longer cyanotic, and the pulse on that side was of good quality, with a rate of 118 per minute. The blood pressure was unobtainable from the right arm; it was 120 systolic and 75 diastolic on the left side.

The patient's color slowly improved. Respirations became less labored, and for a short time the right side of the face drew up into a contracture with the right eye closed and the right corner of the mouth drawn upward. In response to painful stimuli she moved the left side of the mouth. She moved the left arm rapidly in response to painful stimuli and began to move the right arm slowly. She occasionally moved the toes of the right foot; the left lower extremity was moved freely, but the cast made detailed examination of the right leg impossible.

At 5:25 p. m. she moved both upper extremities in response to verbal orders and obviously recognized her own name when it was spoken. She appeared unable to make any verbal reply to questions although able to execute simple commands.

At 5:30 p. m., one hour after the onset, pulsations were not palpable in either the right radial or the right brachial arteries; a feeble pulsation was detectable in the right axillary and temporal arteries, and a moderate pulsation was present in the right carotid as compared with strong pulsations in all comparable arteries on the left side. The radial pulse rate on the left side was 118 per minute. The blood pressure could not be elicited from the right arm but was 120 systolic and 65 diastolic on the left. The lips were still cyanotic. The right upper extremity and the toes of the right foot were still cyanotic and cold, while both left extremities were of normal color and warm.

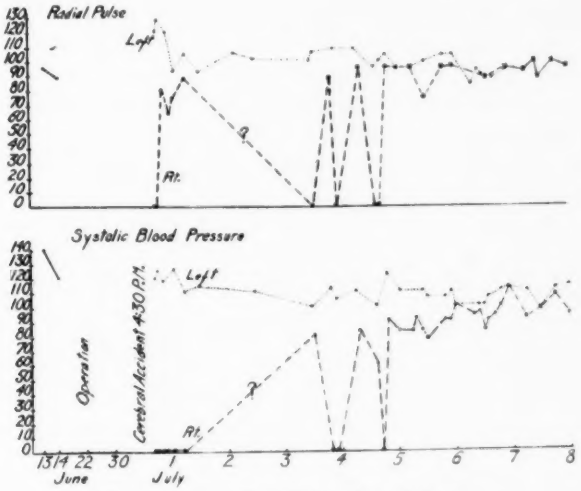
Numerous observations on the blood pressure and radial pulse of both arms were made during the next few days. These are best shown in the accompanying

The Blood Pressure on the Right and Left Arms, the Radial Pulse and the General Body Temperature for Fifteen Days Following the Cerebral Accident

Date	Blood Pressure*		Pulse		Temperature, F.
	Right	Left	Right	Left	
6/13/32 auto accident					
	140/80		96		98.6 (mouth)
6/14/32.....	120/74		88		98.6 (mouth)
6/22/32 operation.	Suture crucial and internal lateral ligaments of right knee				
6/23/32.....	Not taken	Not taken	112		100.6 (mouth)
6/29/32.....	Not taken	Not taken	100		100.6 (mouth)
6/30/32					
4:00 p. m.....	.....	.....	90		100.4 (mouth)
4:30 p. m. cerebral accident					
5:00 p. m.....	Unobtainable	120/70	Unobtainable	120	
6:00 p. m.....	Unobtainable	125/65	Unobtainable	128	
8:30 p. m.....	Unobtainable	118/70	80	116	101.6 (rectal)
9:30 p. m.....	Unobtainable	118/80	64	120	
7/1/32					
12:30 a. m.....	Unobtainable	126/78	76	92	100.8 (rectal)
5:00 a. m.....	Unobtainable	110/70	88	104	99.4 (rectal)
12:00 noon.....	Unobtainable	114/72	Not taken	92	99.4 (rectal)
7/2/32					
11:00 a. m.....	Not taken	110/72	Not taken	102	101.4 (rectal)
7/3/32					
11:00 a. m.....	Not taken	100/68	Not taken	100	101.2 (rectal)
12:10 p. m.....	80/50 (?)	100/68	Unobtainable	106	
8:00 p. m.....	Unobtainable	112/68	88	108	102.4 (rectal)
10:00 p. m.....	Unobtainable	104/66	Unobtainable	108	(Felt as if would faint)
7/4/32					
6:00 a. m.....	84/60 (very faint)	110/70	96	108	101 (rectal)
3:00 p. m.....	60/? (faint)	100/64	Unobtainable	96	101 (rectal)
5:00 p. m.....	Unobtainable	98/78	Unobtainable	100	
8:00 p. m.....	90/70	122/76	96	104	101.4 (rectal)
7/5/32					
12:45 a. m.....	84/70	110/30	96	96	100.6 (rectal)
6:00 a. m.....	84/60	90/54	96	96	
8:00 a. m.....	92/64	92/72	Unobtainable	90	
10:00 a. m.....	84/66	110/72	Not taken	Not taken	
12:00 noon.....	78/66	106/70	76 (?)	100	
8:00 p. m.....	90/66	106/60	96	104	101 (rectal)
10:00 p. m.....	90/56	100/70	Irregular	104	
12 midnight....	100/70	100/56	96 (?)	104	100 (rectal)
7/6/32					
8:00 a. m.....	94/66	100/64	Not taken	84	
10:00 a. m.....	96/72	100/66	Not taken	92	
12:00 noon.....	84/54	100/66	Not taken	90	99.4 (mouth)
2:00 p. m.....	90/66	106/76	88	88	
			Pulse good quality on both sides		
5:00 p. m.....	94/66	108/76	96	88	
8:00 p. m.....	100/74	110/68			
10:00 p. m.....	112/70	112/86	96	94	99.4 (mouth)
7/7/32					
6:00 a. m.....	92/66	110/66	92	92	99 (mouth)
12:00 noon.....	98/66	98/68	88	88	99.2 (mouth)
6:00 p. m.....	108/68	112/72	100	100	
12:00 midnight.	94/84	114/76	92	96	
7/8/32					
12:00 noon.....	92/60	108/70	Not taken	Not taken	99 (mouth)
6:00 p. m.....	108/70	104/66	100	100	
10:00 p. m.....	100/70	100/56	96	96	
7/9/32					
6:00 a. m.....	102/62	102/70	96	88	98.8 (mouth)
6:00 p. m.....	104/64	110/70	96	96	
7/10/32					
6:00 a. m.....	102/66	90/68	84	76	
6:00 p. m.....	96/68	94/68	88	88	
7/11/32					
10:00 a. m.....	106/80	114/80	88	96	98.6 (mouth)
10:00 p. m.....	110/74	110/70	96	94	
7/12/32					
10:00 a. m.....	96/60	100/60	96	96	98 (mouth)
7/13/32					
4:00 p. m.....	110/64	116/72	92	96	99.4 (mouth)
7/14/32					
10:00 a. m.....	116/70	110/70	88	88	
2:00 p. m.....	109/66	100/66	92	88	99 (mouth)

* Although blood pressure, pulse and temperature are recorded as having been taken at the same hour that does not indicate that they were taken simultaneously.

table and graph. In the table and graph it will be noted that the right radial pulse, when palpable, during the first few days was reported as slower than the left. There are at least two possible explanations of this. The pulse was often so feeble that an accurate count was impossible (at times this is indicated by a question mark in the table) and under such circumstances one anticipates errors on the side of too low rather than too high a count. There is also the possibility that the strength of all pulsations was not equal; thus some were palpable and others not. There was, however, at no time any other evidence of cardiac irregularity in force or rhythm. It will also be noted that the pulse was at times recorded as being palpable when the blood pressure could not be obtained. This may possibly be explained in two ways. First, the pulse and blood pressure were rarely determined simultaneously, and second, it is a commonplace clinical observation that the pulsations of the radial artery can be palpated after the blood pressure can no longer be determined by auscultation.



Blood pressure and radial pulse of both arms.

The patient rather rapidly recovered the use of the right arm and right side of the face and was able to move the toes of the right foot.

On July 2, the second day after the onset, she became able to speak but could not express herself clearly, although it was obvious that she clearly comprehended what was said to her.

July 3: The right upper extremity was still obviously colder than the left, but readings of the skin temperature were not taken until later.

July 4: All trace of anesthesia had disappeared.

July 6: The temperatures of the skin were accurately recorded for the first time, but there was no significant difference in the temperatures of the two sides, nor was there any palpable difference still present.

July 15: The patient was greatly improved and able to sit up in bed.

July 20: She was able to walk with the aid of crutches.

August 5: She was discharged from the hospital, and there was no remaining evidence of the cerebral accident.

Jan. 29, 1933: The patient was seen in the outpatient department. Her only complaints were occasional "hot flashes" and dizziness. The blood pressure was 145 systolic and 95 diastolic in both arms.

May 29: She reported that she was able to walk twenty-five blocks without discomfort.

COMMENT

1. *Site of Lesion.*—This report is particularly deficient in that information concerning the nature and location of the lesion is lacking. Whether the cerebral damage was secondary to thrombosis, embolism or hemorrhage it is impossible to say. It does, however, seem possible to be more definite concerning the location of the lesion. Almost the only single point from which right hemihypesthesia and hemiplegia and motor aphasia could be produced is the left internal capsule. Unfortunately there is no evidence concerning the visual fields in this case because of the deep coma in the early stages, the unresponsiveness and motor aphasia later, and the rapid recovery subsequently. A lesion sufficient to produce such widespread changes must have produced a functional interruption of the greater portion of the fiber system in the capsular region; thus, this case is useless for the localizing of any function in any one portion of the cerebral hemisphere or cortex. However, it appears justifiable to conclude that the neurologic manifestations were the result of temporary severance of a part of the left cerebral hemisphere from the remainder of the nervous system.

2. *Vasomotor Manifestations.*—The primary concern in this report is with the vascular manifestations, the absence or gross enfeeblement of the pulsation of all the palpable arteries on the upper half of the right side of the body as compared with comparable vessels on the left, the marked cyanosis of the right upper and lower extremities, and the severe, readily perceptible local lowering of the temperature of the skin on the right side of the body, particularly in the distal parts of the extremities. All of these symptoms are most rationally explained on the basis of a partial or complete obstruction of the vascular network, possibly venous as well as arterial, on the right side of the body. Two possible mechanisms of such obstruction present themselves. Theoretically, multiple emboli might give rise to the entire picture, but it is asking too much to believe that a series of emboli were simultaneously discharged and lodged only in the vascular supply of the left internal capsule and the vessels of the right half of the body and in all of these! It will be recalled that the alteration in pulsation occurred in the temporal, carotid, axillary, brachial and radial arteries on the right, and that the right hand and foot were cold and cyanotic. There is no one point at which a single embolus could have lodged and produced this picture. It is beyond belief that a group of emboli could have been simultaneously so ingeniously distributed as to have done so.

The only explanation of the vascular phenomena which remains is that a generalized constriction of the vessels of the right side of the

body occurred, resulting in a functional obstruction. In support of this thesis is the fact that the pulsation of the larger vessels was less affected than that of the smaller, and that the return of pulsation and blood pressure was not abrupt, as though a mechanical obstruction had been suddenly removed, or gradual, as if such an obstruction were slowly canalized or circumvented, but spasmodic and fitful (graph) as would be the case if a functional obstruction were suddenly relaxed only shortly to recur, this procedure occurring over and over again until a normal state of the vessels finally developed. It should be further pointed out that such an obstruction need not be complete; it need only be of such a degree that pulsations of the vessels would not be palpable or would be greatly enfeebled and the blood pressure unobtainable by ordinary clinical methods (an inflated cuff, a mercury manometer and auscultatory examination). It is probable in this particular instance that all circulation was not abolished in the affected extremities.

3. *Relevant Experimental Observations.*—If such an interpretation is to be accepted in this case, an answer must be found to the question: Is such a functional obstruction, such a marked vasoconstriction possible? The experimental data on this point are inadequate. Since the original demonstration by Claude Bernard in 1851 and 1852 that the sympathetic nervous system exercises vasoconstrictor control, much investigative work directed toward elucidation of the function of this system and its mode of action has been done. However, so far as I have been able to learn, no one has ever studied the degree of vasoconstriction that stimulation of the sympathetic innervation to an extremity can produce in a mammal. It has never been demonstrated in mammalian physiology that excitation of the sympathetic supply to a vessel in an extremity can produce complete obstruction of that vessel or an obstruction of such a degree that the pulsations are no longer perceptible and the blood pressure is unobtainable by ordinary clinical methods. Cobb showed that stimulation of the cervical sympathetic chain causes a constriction of the cerebral vessels of 15 per cent of the original diameter, with definite impairment of circulation. Langley, working with curarized frogs, demonstrated that stimulation of the sympathetic nerve supply to the lower extremity produced "complete closing of one or more arteries of the web" of the foot, and, further, that stimulation of the peripheral end of the cut sciatic nerve, all muscular activity being prevented by curara, produced contraction of the arteries and *"more or less widespread cessation of circulation in the web"* (italics in quotations cited are my own). He stated that this had been confirmed by Wharton Jones, Pflüger, Lister, Putzeys and Tarchanow, Nussbaum, Huizinga, Ellis and Arkharoff. Hooker demonstrated that stimulation of the cervical sympathetic chain *"gave unmistakable evidence of constriction of both capillaries and venules"* in the cat's ear. Krogh and his

co-workers, again using the frog, showed that stimulation of the related sympathetic ganglia with induced currents "produces constriction, *often to obliteration,* of the arteries" of the web, and that, further, the capillaries become constricted five to ten seconds after the arteries, though usually not so completely. It thus is apparent from experimental evidence that in the frog's web and in the cat's ear and brain the local nervous mechanism is sufficient to evoke a vasoconstriction which will abolish or greatly impair circulation. In addition it is a common surgical experience in both the experimental animal and man that during periarterial sympathectomy the mechanical irritation of stripping the artery provokes a marked local vasoconstriction, to such a degree that the vessel looks like a pale cord, all circulation through it temporarily ceases, and all pulsation peripheral to that point disappears (Gask and Ross). This is further evidence that the contractile elements of the wall of a blood vessel are capable of obliterating the lumen.

4. *Relevant Clinical Observations.*—The question then becomes that of whether a cerebral lesion may in some manner evoke this degree of peripheral vasoconstrictor activity. The clinical observations of Zenner and Kramer furnish evidence in favor of this possibility and will therefore be quoted at some length.

> Their patient, a man, aged 57, was apparently well until 1896, when at the age of 45 he suffered for the first time from a convulsive seizure which began as a localized convulsion of the right leg and subsequently became generalized. During the next twelve years there gradually developed a hemiparesis and impairment of sensation on the right side of the body, of the type commonly attributed to a cortical lesion. On May 5, 1909, he was operated on. The tumor, a meningioma, of the left central region was found, and during manipulation of it the *radial pulse disappeared from the right side while remaining of good quality on the left.* The operation was interrupted without removing the tumor. The following day the pulse was equal on the two sides. Three days following the first operation, on May 8, 1909, the patient was operated on a second time. On this occasion the tumor was removed, and during this procedure the pulse was again abolished on the right, and again on the day following operation was equal on the two sides. At no time was the blood pressure recorded.

This case seems to present definite evidence that alterations within the cerebral hemisphere are capable, in a manner not understood, of evoking a contralateral vasoconstriction sufficient to abolish the pulsations of peripheral vessels. The phenomenon noted by these observers must have been of nervous origin; emboli could not explain what occurred. And, of perhaps equal interest, this case demonstrates that in man the cerebral innervation of the vasoconstrictor mechanism is in a large measure lateralized, and that so far as the cerebrum is concerned vasomotor responses need not be of a diffuse widespread character. Observations of this type should be repeated and more extensive and accurate data collected.

5. *Physiologic Interpretation.*—Since these two clinical cases suggest that the peripheral mechanism is capable of producing a functional obliteration of the vascular system sufficient to abolish the pulse and blood pressure, and that cerebral lesions are capable of evoking such a response, it will be interesting to discuss, from the standpoint of experimental and clinical data, the possible mode of action of the cerebral influence. The ability of the various lower portions of the nervous system to maintain their physiologic activities at practically normal levels after having been deprived of their higher centers is a phenomenon found to a striking degree in the sympathetic portion of the mammalian nervous system. Although removal of the sympathetic ganglia or section of the efferent sympathetic trunk results in vasodilatation (loss of the normal degree of vasoconstriction), this is temporary and within a few days the vessels have resumed their previous caliber and the temperature of the skin, elevated by the vasodilatation, resumes the normal level (Goltz, Krogh, Kuntz), although some workers have found more persistent vasodilatation under some circumstances. The same ability to maintain vasomotor activity and to respond in a relatively normal but diminished reflex manner is found in the spinal cord isolated from the brain (Goltz, Sherrington, Brooks). Section of the spinal cord in the lower cervical region produces a severe fall of general arterial tension, and vasomotor reflexes can no longer be elicited. In a few days the blood pressure returns to normal, and the vasoconstrictor reflexes, though slightly diminished in amplitude, are again readily obtained. Thus "vasomotor center or centers" capable of autonomous activity are demonstrable within the spinal cord.

Owsjannikow, Dittmar, Ranson and Billingsley, and Scott and Roberts have demonstrated like centers within the floor of the fourth ventricle. However, as Brooks pointed out for centers in this area concerned with reflex control of blood sugar, the demonstration of such centers does not indicate that still higher centers have no ability to exert further control. As Dittmar and Owsjannikow have shown that successive sections of the brain stem from above downward do not produce a fall in blood pressure until the medulla is reached, it seems likely that the medullary centers are primarily concerned with the maintenance of a certain "normal" vasoconstrictor state, and that higher centers are primarily concerned with phasic reflex activity in response to uncommon conditions and stimuli. Much of the existing experimental work supports this point of view.

In 1918, Karplus and Kreidl, contrary to their previous observations, found that in some instances electrical stimulation of the hypothalamus in curarized animals produced definite increases in the general arterial tension. In 1927, they reported a second series of similar experiments which confirmed their earlier work. In addition, they determined that

the rise in blood pressure occurs after removal of the hypophysis and suprarenals. It was therefore assumed that the rise was due to vasoconstriction mediated by the sympathetic nervous system. This thesis was supported by the appearance of other evidences of sympathetic activity (dilatation of the pupil and retraction of the nictitating membrane) when this area was stimulated. In 1928, Wang and Richter reported that "in a series of fifteen animals we were able to confirm Karplus and Kreidl's findings with regard to the pupils, nictitating membranes, lacrimal glands and general arterial blood pressure." In addition they reported other evidence of sympathetic activity from such stimulation, increased secretory activity of the sweat glands of the foot-pad, as evidenced by changes in action potentials in the skin. The latter effect was abolished by section of the sympathetic nerves to the foot or of the brain stem below the hypothalamus. In 1930, Beattie, Brow and Long further confirmed these findings by demonstrating that stimulation of a small, sharply limited area in the posterior hypothalamus produced a rise in the general blood pressure and evoked extrasystoles. In 1932, Beattie stated that stimulation of this area increased the general blood pressure, increased the heart rate, dilated the pupils and produced pilomotor effects. Recently, Ranson, Kabat and Magoun also reported the elicitation of sympathetic responses such as dilatation of the pupils and a rise in blood pressure, accompanied by an increase in rate and depth of respiration, from stimulation of the hypothalamus in cats.

Leiter and Grinker attempted to repeat this work recently, but were unable to confirm it. However, such a mass of positive data from various laboratories leads one to doubt the significance of negative evidence. Leiter and Grinker elicited rises in the general blood pressure in many of their animals, but attributed that either to muscular activity or apnea. However, in at least one of their experiments (cat 7) there was no muscular activity or apnea and yet rises in the blood pressure of from 14 to 33 mm. of mercury were obtained on stimulation of the posterior hypothalamus. There were other similar isolated instances. Also there were a number of experiments in which definite muscular activity and/or apnea was associated either with no rise or with an actual fall in blood pressure. It thus becomes doubtful whether their conclusions that such rises in blood pressure as they obtained are due to muscular activity or apnea can be accepted. Their conclusions become even more unacceptable in view of Brooks' work in which he showed that muscular activity may not evoke any marked alteration in the general blood pressure. It should be recalled that stimulation of the hypothalamus is associated with other evidences of sympathetic activity in addition to vasoconstriction, such as sweating, pupillary phenomena, pilomotor activity, cardiac acceleration, cardiac extra-

systoles, etc. It is certain that these authors would not attribute all of these phenomena to muscular activity and apnea. Yet it seems unlikely that these manifestations of sympathetic activity could be elicited from the hypothalamus and not vasoconstriction.

Other evidence of the control of sympathetic activity by the hypothalamus has been presented by Bard. He demonstrated that decorticate cats were subject to attacks which occurred spontaneously or could be precipitated by slight peripheral stimulation. These attacks, referred to as "sham rage," were characterized by struggling, arching of the trunk, thrusting and pulling of the limbs with protrusion of the claws, lashing of the tail, snarling expression, panting, pilo-erection, sweating of the toe-pads, retraction of the nictitating membrane, exophthalmos and a marked increase in arterial pressure and cardiac rate. He stated that similar phenomena have been observed to a greater or less extent by Goltz, Rothman, Dusser de Barenne, and Cannon and Britton. These phenomena disappeared, at least in such a marked and definite form, on removal of the hypothalamus. Further, Cannon and Britton showed that some of these phenomena, notably sweating, disappeared from the forelimbs on removal of the stellate sympathetic ganglia, thus demonstrating that the phenomena are not "humoral." In addition, Wang and Richter noted spontaneous increase in the secretory activity of the foot-pad, as determined by measurement of action potentials, in thalamic animals as evidence of increased sympathetic activity comparable to sham rage and this, too, they showed to disappear with sympathetic ganglionectomy.

It is true that Woodworth and Sherrington elicited a condition similar to sham rage in animals from which the cerebrum and thalamencephalon had been removed. It is possible, however, that small portions of the posterior hypothalamus may have been left intact in their animals. The "sham rage" was very mild and of brief duration, and was elicited only by painful stimulation, whereas true sham rage occurs spontaneously or on the slightest, not at all painful, stimulation. Keller also elicited a certain mild type of "sham rage" in midbrain animals but it never occurred spontaneously and was less pronounced than in thalamic animals.

From this it appears that within the hypothalamus is a mechanism which functions as the "central ganglion" of the sympathetic nervous system but which is under the inhibitory control of some higher center within the cerebral cortex. When that higher center is removed by decortication it releases the diencephalic and lower mechanisms to explosive activity. A similar function has been attributed to the cortex by many writers, including Beattie, Brickner, and Langworthy and Richter.

These experimental facts and the conclusions drawn from them may now be related to the phenomena observed in the case presented here. It may be supposed that a lesion in the internal capsule of the left cerebral hemisphere produced a temporary functional block of the inhibitory impulses descending from the cerebral cortex to the vasoconstrictor centers of the hypothalamus and the medulla, and that these centers released from inhibitory control expressed their overactivity in an intense constriction of the vessels of the right side of the body. This sympathetic overactivity was manifest in waves of vasoconstriction, much as Bard's decorticate cats gave vent to spontaneous attacks of sham rage, as is obvious from the graph of the blood pressure determinations. The nature of the stimulus which induced these attacks of hyperactivity is, of course, unknown, but Bard has demonstrated the mild and inocuous character of the stimuli sufficient for that purpose.

In only one main point is the correlation of this clinical case and the physiologic evidence still defective. The responses demonstrated in laboratory animals are for the most part diffuse generalized responses; those seen in this case were almost exclusively unilateral. It is true that the lips were cyanotic, and there was a slight temporary cyanosis of the left upper extremity. That, however, may have been due to poor aeration of the blood as a result of the labored respirations. Such an explanation will not, however, account in any measure for the changes on the right side. But the physiologic experiments are not entirely devoid of evidence of lateralization of function. Karplus and Kreidl demonstrated that the efferent vasoconstrictor fibers within the spinal cord are largely ipsilateral, while Ranson and Hess showed the afferent pressor fibers to be chiefly ipsilateral and the depressor fibers contralateral within the spinal cord. Karplus and Kreidl also demonstrated that on exciting the hypothalamus with weak stimuli the effect, in the cat, is prompter in the contralateral eye. They also stated that in monkeys (Macacus rhesus) the results of stimulation of the hypothalamus are more definitely contralateral than in cats. Fulton, Kennard and Watts also found, in monkeys, that the cortical influence over the vasomotor mechanism is primarily evident in the contralateral extremities. This increase in lateralization in the brain of the monkey as compared with the cat is not surprising, as it is in agreement with findings relative to the cortical motor projection system (Bucy and Fulton). And it is to be anticipated that in man the independence of the sympathetic innervation of one side of the body from that of the other would be still greater, as is true of other forms of cortical activity.

6. *Vasomotor Phenomena from Cortical Stimulation and Ablation.*—At this point a brief consideration of the studies of the vasomotor mechanism from stimulation of the cerebral cortex is perhaps not amiss, although the experiments are on the whole so unsatisfactory and the

results so inconclusive as to make them of little value. Brown-Séquard, in 1875, reported that cauterization of the superior surface of the cerebrum produced changes in the structures of the head on the same side, comparable to those seen on section of the cervical sympathetic. That these phenomena were the result of peripheral factors rather than cerebral irritation or destruction is attested by the fact that the cauterization was associated with convulsive movements of the face of the same side, and that comparable results were obtained from cauterization of the scalp, pericranium and meninges. Bochefontaine in the following year reported that faradization of the cortex produced increased intra-arterial tension and slowing of the pulse, but he obtained the same results from similar stimulation of the dura mater and sciatic nerve, thus demonstrating that the results were secondary to the stimulation of sensory nerves rather than to that of the cerebral cortex. The results of the spread of a strong faradic current, on stimulation of the cerebral cortex, to neighboring sensitive structures are familiar to all workers experienced in this field of physiology. The experiments of Eulenberg and Landois reported in 1876 are somewhat more convincing, but confirmatory investigation is sorely needed. They found that extirpation of a portion of the canine cerebral cortex near the cruciate sulcus caused a rise in temperature in the contralateral extremities, and that stimulation of this area produced a fall in temperature. This would indicate an area in the cortex concerned with the stimulation of the vasoconstrictors or the inhibition of the vasodilators. However, this isolated bit of evidence out of harmony with the main body of experimental data will have to await confirmation before it will be acceptable. Bechterew and Misslawsky, in 1886, reported that in curarized cats and dogs electrical stimulation of the sigmoid gyrus produced an increase in blood pressure while stimulation of the parietal lobe caused a decrease. However, as they found that stimulation of a multitude of cortical areas evoked changes in blood pressure it would appear likely that their results, like those of Bochefontaine, were probably due to spread of current to sensory nerves in the meninges. François-Franck criticized the work of previous investigators as being unreliable and then reported experiments of his own which showed that stimulation of the marginal convolution evoked a vasoconstrictor response. Schäfer cited the references just mentioned and added the observations of Schiff and Vulpian without mentioning their findings, and of Danilewsky and Richet who obtained vasoconstriction. Schäfer and Bradford constantly obtained vasodilatation from stimulation of the mesial surface of the hemisphere anteriorly in monkeys, and vasoconstriction from some other parts of the cerebral cortex. It is obvious from this brief review that the results of cortical stimulation are in this regard totally inadequate and unconvincing. Although it is entirely

possible, on theoretical grounds alone, that there are both a vasoconstrictor and a vasodilator center within the cerebral cortex, the existence of such centers is as yet unproved.

CLINICAL LITERATURE

A review of the literature reveals that the observation of vasomotor disturbances in association with cerebral hemiplegia is by no means new. One of the earliest references to this subject is the thesis of Chevallier, published in 1867, which is entirely devoted to the subject of paralysis of the vasomotor system in hemiplegia. It is obvious from his report that his preceptors were quite familiar with these manifestations and in all probability published reports which were not found in this review (Gubler, 1856).

Many reports are concerned with manifestations of involvement of the sympathetic nervous system other than vasomotor, but I have confined my attention as much as possible to evidence of vasomotor disturbances. These are primarily of two classes, changes in the caliber of the vessels as shown by local changes in the pulse and blood pressure, and changes in the local temperature of the skin, which are largely secondary to vasomotor alterations, although excessive or diminished local sweating may also be a factor in some instances. It is natural, of course, that in many of these reports reference to other less definite and less accurately measurable secondary phenomena, such as cyanosis and edema, should be made, as well as to other manifestations of disturbed functioning of the sympathetic system, such as sweating, trophic changes in the skin, pilomotor activity, etc.

On the whole, one is impressed with the indefiniteness and variability of these manifestations. And, in order to evaluate best the multitude of reports, a brief consideration of comparable findings in normal persons may prove of value. In this connection a report by Claus and Bingel on a study of normal variations of the temperature of the skin and others by Fischer and Hensen on the blood pressure simultaneously taken on the two arms of relatively healthy persons are particularly interesting.

Claus and Bingel, using a mercury thermometer especially made for their purposes, found that in healthy persons the temperature of the skin taken at symmetrical points on the two sides of the body simultaneously often varied as much as 1 C. Fisher studying the blood pressure in the two arms of eighty convalescent patients or persons who had been subjected to minor surgical procedures made some two hundred and seventy observations. In sixty-three observations the readings were taken simultaneously in the two extremities, but the results were the same as in the others. He found that in only 13 per cent of the observations were both systolic and diastolic readings the same

in the two upper extremities. In the remaining readings the differences were usually only from 5 to 10 mm. of mercury, although in apparently healthy persons differences of as much as 30 mm. of mercury were seen; while in persons with arterial hypertension the differences were of greater magnitude, often reaching as high as 40 mm. of mercury in the systolic and 20 mm. in the diastolic readings. The higher readings were about equally divided betweeen the right and left sides. Hensen stated that differences between the readings of blood pressure in the two arms of from 1 to 3 mm. are common, differences of from 8 to 10 mm. are seen, and in cases of arteriosclerosis differences of as much as 18 mm. were found. It must be obvious, therefore, that minor differences between the hemiplegic and the nonparalyzed side (and these constitute the great majority of those reported) are of little or no significance. This also explains in part why the reported findings are at such variance. In addition, it is to be recalled that practically all observations reported were made on patients months or even years after the onset of the hemiplegia. This is in striking contrast to the study of the case reported by Zenner and Kramer and to that of the case reported here, in both of which observations began with the onset of the vasomotor phenomena. Studies made on patients with chronic hemiplegia suffer from two main difficulties. First, the ability of the vasomotor mechanism to adjust itself to the removal of the higher integrative centers (Goltz, Sherrington), even to adjust itself to the destruction of the centers within the spinal cord (Goltz) and even to that of the sympathetic ganglia (Krogh, Kuntz) is truly remarkable. Thus, any vasomotor manifestations which may be present at the onset of the hemiplegia must largely disappear with the passage of time, and the changes which subsequently develop may be in a large measure secondary to the state of the paralyzed extremity. What effect disuse, the constant retention of the extremity in one position, spasticity or flaccidity of the muscles, the protection of the extremity in part from the constant flood of external stimuli which a normally functioning member receives have on the vascular network has not as yet been clearly evaluated. In this connection the observations of Kahler are of interest. He studied fifty-five cases. In twenty-six the hemiplegia was said to have been due to cerebral hemorrhage, in eighteen to cerebral thrombosis, in nine to embolism and in two to tumors. However, as only sixteen cases came to autopsy there may be occasion for doubt as to the accuracy of the pathologic diagnoses in some instances. Of the fifty-five patients, five had contractures, and in these the blood pressure was lower on the affected side. In forty-nine patients in whom the blood pressure was higher on the affected side the paralysis was said to be flaccid (*"die Lähmung bei den übrigen Kranken eine schlaffe war"*), although it must be obvious that he refers

not to a true flaccid paralysis but only to relative flaccidity as compared with the older cases with marked contractures, for it is inconceivable that forty-nine of fifty-five patients with cerebral hemiplegia should have flaccid paralysis unless they were observed at the onset of the condition, and there is no evidence that they were. However, it should be pointed out that in the main the differences which Kahler found, from 10 to 20 mm. of mercury in the majority of instances, occasionally as much as 30 mm. of mercury, are within the limits of normal found by Fischer.

A study of the multitude of cases of hemiplegia reported in the literature in which the arterial tension on the two sides was studied reveals that a majority of the authors (ten) found the arterial tension to be lower on the hemiplegic side (Oppenheim, Melchior and Wilimowski, Aguglia and Leanza, Hecht and Langstein, Féré, Villard, Sicard and Guillain, Marinesco, Tixier and Mirallié). Six (Fischer, Parhon and Papinian, Goldstein, Peritz, Raymond and Schrottenbach) found it to be higher. Fischer, however, pointed out that in the majority of cases the variation was not constant and too slight to be of significance. Villaret and Théodoresco, Villaret and Jonesco, Daniélopolu, Radovici, Carniol and Aslan and Friedlander thought any changes observed too slight and too variable to have significance. Pal found no differences on the two sides. Ratky and Klein studied four cases and found the tension higher on the involved side in three, lower in one. Kahler concluded, as already noted, that the blood pressure was lower in the presence of contracture, higher in relatively flaccid extremities. Villaret and Théodoresco, on the other hand, although impressed with the inconstancy of the findings, thought that the pressure tended to be higher in cases with contracture and lower in those with flaccidity. Probably in agreement with these findings is Rimbaud's statement that the pressure on the paralyzed side is lower than normal in recent cases, higher in old ones. Böwing studied twelve cases and found the tension on the hemiplegic side higher in five, lower in five and the same as on the uninvolved side in two.

It seems apparent that with such marked discrepancies in the observations of so many workers these data are of little significance for the interpretation of the cerebral mechanism of vasomotor control. This is even more apparent when one investigates the magnitude of the difference in arterial tension with which these authors are dealing. Kahler found differences of from 10 to 20, occasionally as much as 30 mm. of mercury; Böwing, differences of from 5 to 20, in one instance 35 mm. of mercury. Ratky and Klein found differences of 10, 20, 20 and 60 mm. in four cases. Villaret and Jonesco found differences of from 5 to 20 mm. and commented on the variability of these findings. Mirallié found differences of 10 mm. in eight cases,

20 in six, 30 in two, 40 in two others; Schrottenbach, differences up to 12 mm. of mercury; Peritz, differences of from 10 to 20 mm., and Melchior and Wilimowski, a decrease of 30 mm. in one case, whereas in their other case the blood pressure was unobtainable on the paralyzed side though the systolic arterial tension was determined at 103 mm. of mercury on the sound side. The last is, so far as I have been able to find, the only example in the literature of a completely unobtainable blood pressure in an extremity presenting an old (duration sixteen months) hemiplegia. When one recalls that Fischer commonly found variations of as much as from 5 to 10 mm. of mercury and not uncommonly differences of as much as 30 mm. of mercury in the arterial tension of the two arms of healthy subjects, and of as much as 40 mm. in cases of arterial hypertension, it is at once apparent that for present purposes this entire vast literature must be discarded.

The observations in regard to changes in the local temperature of the skin in hemiplegia are much more consistent. Oppenheim, according to Claus and Bingel, observed that in early cases the temperature is higher on the paralyzed side whereas it is lower in old cases. In this observation he has been confirmed by Chevallier, Schüller, Guicciardi and Petrazzani, Pontoppidan and Bock and Cabet. Only a decrease in the local temperature of the skin was reported by Böwing, Villaret and Jonesco, Bikeles and Gerstmann, Rossolimo, Féré and Olsen. However, they were all dealing with cases of long standing. Gubler is reputed to have found a rise in the temperature of the skin on the affected side, although no information is available as to how long after the onset of the condition the observations were made, and Nothnagel found an increase in local temperature on the affected side some eleven weeks after the development of hemiplegia.

The magnitude of the differences in temperature on the two sides seems to be great enough in the majority of instances in which definite data are available to make the observations significant in view of the finding of Claus and Bingel that variations between the two sides of apparently normal persons were 1 C. or less. Biach and Bauer found increases of from 0.2 to 0.9 C. and decreases of from 0.2 to 2.6 C.; Rossolimo found the involved extremities to be from 2 to 3 C. cooler. Chevallier found increases of from 0.15 to 3.2 C.; Schüller, of 2 C.; Guicciardi and Petrazzani, of from 0.7 to 2.3 C.; while Olsen recorded decreases of from 0.2 to 5.2 C. In view of the fact that practically all of the determinations were made with mercury thermometers the accuracy might be questioned.

The rise in local temperature so commonly observed early in cases of hemiplegia might be due either to vasodilatation or to diminished local perspiration. Its occurrence might therefore be used as an argument for either increased or decreased sympathetic activity. The fall

in local temperature which is an almost constant finding in hemiplegias of long duration is in all probability due in part to the inactivity of the extremity with the resultant inactivity of the vascular system and also probably in a large measure to the increased local sweating which is so common in these cases (Nothnagel, Charcot, von Leube, Seeligmüller, Parhon and Goldstein, Bickeles and Gerstmann, Peritz and Bichat). This increased perspiration may be evidence of increased activity of the sympathetic nervous system, and probably is, but the possibility exists that the parasympathetic system may produce similar effects. Brickner has produced additional evidence, increase of pilomotor activity on the paretic side of the body, of augmentation of the reflex activity of the sympathetic nervous system in comparable cases.

Other evidences of altered vasomotor activity, the import of which is less clear, are alterations in color of the paralyzed extremities as reported by Mager, Oppenheim, Bickeles and Gerstmann, Peritz, Rossolimo, and Guicciardi and Petrazzani. In the majority of instances the extremities are recorded as cyanotic, although Bikeles and Gerstmann referred to them as red; Oppenheim stated that at times they are red, while Guicciardi and Petrazzani spoke of them as pink. This change in color of the extremities is probably due to a vascular stasis secondary to vasoconstriction not only of the arteries but of the veins as well. This condition also may be due to hyperactivity of the sympathetic system, as stimulation of the sympathetic chain has been shown to result in a venous as well as an arterial spasm (Hooker).

A few authors have referred to a condition known as "vasomotor epilepsy" (Oppenheim). Mager recorded such a case, associated with a gumma in the right lower postcentral area, in which convulsions, preceded by an aura of paresthesias in the left hand, began with spasmodic movements of the left hand which spread up the arm to involve the entire body and were associated with a sudden fall in the temperature of the skin of the left hand and forearm and increased sweating of that part. Meige and Benisty (1917) and Benisty (1918) recorded five cases of slightly different type. The five patients, all suffering from traumatic injury of the brain, presumably in the rolandic area, were subject to attacks of localized vasomotor spasm in which the upper extremity became cold and cyanotic. These attacks were associated with a gradually developing enfeeblement of the extremity which the authors interpreted as due to the localized ischemia resulting from the vascular spasm. It seems likely that these paroxysmal vasoconstrictive phenomena were evidence of a hyperresponsive sympathetic nervous system reacting unduly in the absence of higher inhibition (cerebral cortex), just as Bard's decorticate cats responded paroxysmally with sympathetic overactivity when properly stimulated.

The data concerning localized edema are less clear. This condition has been recorded in instances of hemiplegia by Oppenheim, Mirallié, Marie, Marinesco, Loeper and Crouzon, Deumie, Euzière, Heitz and de Jong, Rossolimo, Nothnagel, and Guicciardi and Petrazzani. Nothnagel recorded an interesting case in which a patient with nephritis ("Bright's disease") suffered a hemiplegia two years after the onset of the nephritis. Only the affected extremities became edematous, so much so that they were painful. Some three months later the unilateral edema was still present, the thigh was massive, there was marked edema of the involved (right) upper extremity, and there was slight ascites. In addition, all the usual findings of a hemiplegia of the right side were present, with hypalgesia on the right side. Mirallié also recorded an instance of unilateral edema in hemiplegic extremities. The involved left lower extremity was 4 cm. larger than the right. This had been present for a year, the patient suffering, in addition to the hemiplegia, from cardiac disease. Mirallié stated that Pierre Marie always insisted that the localized edema in hemiplegic extremities in cases of cardio-renal disease was due to the inactivity and posture of the extremities. Mirallié was of the opinion that it was due to vasomotor disturbances. It is obvious that this question cannot be settled here. Even if one assumes that the disturbance is on a vasomotor basis it is not apparent whether it is due to stasis within the vascular system from venous constriction (sympathetic hyperactivity) or from dilatation of the entire vascular bed (sympathetic inactivity).

From this review of the literature it seems that a few conclusions may be drawn.

1. The local temperature of symmetrical points on the two sides of the body may vary as much as 1 C. in apparently normal persons.

2. The blood pressure in the two arms may differ by from 5 to 30 mm. of mercury in healthy persons, and by as much as 40 mm. in patients with arterial hypertension.

3. The arterial tension in hemiplegic extremities as compared with those on the unaffected side may be higher, lower or the same, but in any case the variation when the hemiplegia has become chronic is rarely of sufficient magnitude to be of significance.

4. Early in cases of hemiplegia the temperature of the skin is commonly higher on the affected side than on the other, whereas in chronic cases the hemiplegic side is the cooler. And this evidence, as has been pointed out, is of little value in determining the functional state of the vasomotor mechanism.

5. Excessive pilomotor reflex activity on the hemiparetic side has been recorded. This is undoubtedly an evidence of increased reflex activity of the sympathetic nervous system.

6. Changes in color, cyanosis and localized edema in the hemiplegic extremities have been described, but their significance, so far as the sympathetic nervous system is concerned, is uncertain.

SUMMARY

A case of suddenly developing right hemiplegia, hemihypesthesia and motor aphasia has been described. It was observed almost from the onset. Although the imperfections of the observations are realized it is hoped that they may stimulate further reports of vasomotor changes observed early in cases of hemiplegia. Marked manifestations of vasoconstriction involving the right side of the body were present. During the course of several days these fitfully subsided and the vasomotor state returned to normal, somewhat slower than did the hemiplegia, hypesthesia and aphasia.

After a brief review of other pertinent clinical cases and the experimental data it is thought that these phenomena were most probably the result of functional interruption of inhibitory fibers from the cortex to the vasoconstrictor centers of the hypothalamus and medulla, with a release of those structures to explosive overactivity and hyperreflexia.

The extensive clinical literature dealing with supposed vasomotor changes in cases of hemiplegia has been reviewed. The insignificant character of many of the alterations reported, as well as the uncertainty of their relationship to the central vasomotor mechanism, and the fact that many of them are in direct contradiction to the observations of other workers have been pointed out. This material is on the whole of little value in elucidating the mechanism of central vasomotor control.

BIBLIOGRAPHY

Aguglia and Leanza, cited by Fischer.

Bard, P.: A Diencephalic Mechanism for the Expression of Rage with Special Reference to the Sympathetic Nervous System, Am. J. Physiol. **84**:490, 1928.

The Central Representation of the Sympathetic Nervous System as Indicated by Certain Physiological Findings, in The Vegetative Nervous System, Association for Research in Nervous and Mental Diseases, ser. research publ., 1928, vol. 9, p. 67, Baltimore, Williams & Wilkins Company, 1930.

Beattie, J.: Hypothalamic Mechanisms, Canad. M. A. J. **26**:400, 1932.

——Brow, G. R., and Long, C. N. H.: The Hypothalamus and the Sympathetic Nervous System, in The Vegetative Nervous System, Association for Research in Nervous and Mental Diseases, ser. research publ., 1928, vol. 9, p. 249, Baltimore, Williams & Wilkins Company, 1930.

Physiological and Anatomical Evidence for the Existence of Nerve Tracts Connecting the Hypothalamus with Spinal Sympathetic Centers, Proc. Roy. Soc., London, s.B **106**:253, 1930.

Bechterew, W., and Misslawksy: Ueber den Einfluss der Grosshirnrinde auf den Blutdruck und die Herzthätigkeit, Neurol. Centralbl. **5**:193, 1886.

Benisti: Les lésions de la zone rolandique (zone motrice et zone sensitive) par blessures de guerre, Thèse de Paris, 1918.

Bernard, C.: Influence du grand sympathique sur la sensibilité et sur la calorification, Compt. rend. Soc. de biol. **3**:163, 1851.

Sur les effets de la section de la portion céphalique du grand sympathique, ibid. **4**:168, 1852.

Biach, P., and Bauer, J.: Ueber Störungen der Temperaturregulierung bei Nervenkrankheiten; eine Methode für die Funktionsprüfung der Vasomotoren, Deutsche Ztschr. f. Nervenh. **41**:464, 1911.

Bichat, cited by Raymond.

Bikeles, G., and Gerstmann, J.: Ueber die vermehrte Schweissabsonderung auf der gelähmten Seite (nach Pilokarpininjektion) bei kortikalen Läsionen, Neurol. Centralbl. **34**:770, 1915.

Bochefontaine: Etude expérimentale de l'influence exercée par la faradisation de l'écorce grise du cerveau sur quelques fonctions de la vie organique, Arch. de physiol. norm. et path. **3**:140, 1876.

Böwing, H.: Störungen der Gefässfunktion, der Schweissabsonderung, der Piloarrektion und der Trophik nach organischen Nervenschädigungen, Klin. Wchnschr. **2**:2117, 1923.

Brickner, R. M.: Certain Charcteristics of the Cortical Influence Over the Sympathetic Nervous System in Man, J. Nerv. & Ment. Dis. **71**:689, 1930.

Brooks, C. M.: Reflex Activation of the Sympathetic System in the Spinal Cat, Am. J. Physiol. **106**:251, 1933.

A Delimitation of the Central Nervous Mechanism Involved in Reflex Hyperglycemia, ibid. **99**:64, 1931.

Brown-Séquard, C. E.: Recherches sur l'excitabilité des lobes cérébraux, Arch. de physiol. norm. et path. **2**:854, 1875.

Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318, 1933.

Cabet, 1926, cited by Olsen.

Cannon, W. B., and Britton, S. W.: Studies on the Conditions of Activity in Endocrine Glands: XV. Pseudaffective Medulliadrenal Secretion, Am. J. Physiol. **72**:283, 1925.

Charcot, cited by Bikeles and Gerstmann.

Chevallier, P. E.: De la paralysie des nerfs vaso-moteurs dans l'hémiplégie, Thèse de Paris, no. 175, 1867.

Claus, R., and Bingel, A.: Ueber Messungen der Hauttemperatur bei Gesunden und Nervenkranken, Deutsche Ztschr. f. Nervenh. **37**:161, 1909.

Cobb, S.: The Cerebral Circulation, in The Vegetative Nervous System, Association for Research in Nervous and Mental Diseases, ser. research publ., 1928, vol. 9, p. 458, Baltimore, Williams & Wilkins Company, 1930.

Daniélopolu, D.; Radovici, A.; Carniol, A., and Aslan, A.: Recherches sur la circulation peripherique chez l'homme, Recherches sur les vasomoteurs droits et gauches dans l'hémiplégie capsulaire et les lésions corticales, J. de physiol. et de path. gén. **24**:541, 1926.

Deumie, cited by Mirallié.

Dittmar, C.: Ueber die Lage des sogenannten Gefässcentrums in der Medulla oblongata, Ber. u. d. Verhandl. d. K. sächsischen Gesellsch. d. Wissensch. zu Leipzig, Math. Phys. Cl. **25**:449, 1873.

Eulenberg, A., and Landois, L.: Ueber die thermischen Wirkungen experimenteller Eingriffe am Nervensystem und ihre Beziehung zu den Gefässnerven, Virchows Arch. f. path. Anat. **66**:489, 1876.

Ueber die thermischen Wirkungen experimenteller Eingriffe am Nervensystem und ihre Beziehung zu den Gefässnerven, ibid. **68**:245, 1876.

Euzière, cited after Mirallié.

Féré, C.: Note sur les rapports qui existent chez les hémiplégiques entre l'atrophie musculaire, la temperature locale des membres et la pression sphygmometrique, Compt. rend. Soc. de biol. **40**:638, 1888.

Fischer, P.: Zur Frage differenter Blutdruckwerte im Bereich verschiedener Gefässgebiete beim Menschen, Klin. Wchnschr. **3**:784, 1924.

François-Franck, C. A.: Influence de l'excitation du cerveau sur les principales fonctions organiques, Compt. rend. Soc. de biol. **40**:27, 1888.

Fulton, J. F.; Kennard, M. A., and Watts, J. W.: Autonomic Representation in the Cerebral Cortex. (In preparation.) Preliminary Report, Proc. Am. Physiol. Soc., 1934.

Gask, G. E., and Ross, J. P.: The Surgery of the Sympathetic Nervous System, Baltimore, William Wood & Company, 1934.

Goldstein, cited by Kahler.

Goltz, F.: Ueber gefässerweiternde Nerven, Arch. f. d. ges. Physiol. **9**:174, 1874.

Gubler, 1856, cited by Chevallier.

Guicciardi, G., and Petrazzani, P.: Delle piu recenti localizzazioni di centri termo-regolatori nel corpo striato, Riv. sper. di freniat. **13**:399, 1887.

Hecht and Langstein: Allg. Wien. med. Ztg. **45**:418, 1900; cited by Kahler.

Heitz and de Jong, cited by Mirallié.

Hensen, H.: Beiträge zur Physiologie und Pathologie des Blutdrucks, Deutsches Arch. f. klin. Med. **67**:436, 1900.

Hooker, D. R.: The Functional Activity of the Capillaries and Venules, Am. J. Physiol. **54**:30, 1920.

Kahler, H.: Ueber vasomotorische Störungen bei zerebralen Hemiplegien, Wien. klin. Wchnschr. **35**:219, 1922.

Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: II. Ein Sympathicuszentrum im Zwischenhirn, Arch. f. d. ges. Physiol. **135**:401, 1910.

Gehirn und Sympathicus: IV. ibid. **171**:192, 1918.

Gehirn und Sympathicus: VII. Ueber Beziehungen der Hypothalamuszentren zu Blutdruck und innerer Sekretion, ibid. **215**:667, 1926-1927.

Keller, A. D.: Autonomic Discharges Elicited by Physiological Stimuli in Mid-Brain Preparations, Am. J. Physiol. **100**:576, 1932.

Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1924.

——Harrop, G. A., and Rehberg, P. B.: Studies on the Physiology of Capillaries: III. The Innervation of the Blood Vessels in the Hind Legs of the Frog, J. Physiol. **56**:179, 1922.

Kuntz, A.: The Autonomic Nervous System, Philadelphia, Lea & Febiger, 1929.

Langley, J. N.: The Origin and Course of the Vaso-Motor Fibers of the Frog's Foot, J. Physiol. **41**:483, 1911.

Langworthy, O. R., and Richter, C. P.: The Influence of Efferent Cerebral Pathways upon the Sympathetic Nervous System, Brain **53**:178, 1930.

Leiter, L., and Grinker, R. R.: Rôle of the Hypothalamus in Regulation of Blood Pressure; Experimental Studies with Observations on Respiration, Arch. Neurol. & Psychiat. **31**:54 (Jan.) 1934.

von Leube, cited by Bikeles and Gerstmann.

Loeper and Crouzon, cited by Villaret and Jonesco.

Mager, W.: Zur Kenntnis vasomotorischer Symptome bei Hirntumoren, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **16**:340, 1907.

Marie, P., cited by Mirallié.

Marinesco, cited by Villaret and Jonesco.

Meige, H., and Benisty, A.: Parésie Jacksonienne, Bull. et mém. Soc. méd. d. hôp. de Paris **41**:1128, 1917.

Melchior, E., and Wilimowski, M.: Ueber das Verhalten des Pulses in gelähmten Gliedmaszen, Zentralbl. f. Chir. **43**:49, 1916.

Mirallié, C.: Contribution a l'étude de la tension artérielle et de l'oedème chez les hémiplégiques, Bull. et mém. Soc. méd. d. hôp. de Paris **44**:889, 1920.

Nothnagel, H.: Betheiligung des Sympathicus bei cerebraler Hemiplegie, Virchows Arch. f. path. Anat. **68**:26, 1876.

Olsen, A.: Hemiplegi og hudtemperatur, Hospitalstid. **76**:1097, 1933.

Oppenheim, H.: Text-Book of Nervous Diseases, translated by A. Bruce, Edinburgh, Darien Press, 1911.

Owsjannikow, cited by Dittmar.

Pal, cited by Kahler.

Parhon and Papinian, cited after Kahler.

Parhon, C., and Goldstein, M.: Sur quelques troubles vaso-moteurs dans l'hémiplégie, România med. **1**:2, 1899; abstr., Rev. neurol. **10**:865, 1902.

Peritz: Zwei Fälle von Gehirnschüssen mit Lagegefühlsstörungen, Astereognosie, trophischen Veränderungen und halbseitiger Blutdrucksteigerung, Neurol. Centralbl. **34**:140, 1915.

Pontoppidan, K.: Lectures on Nervous Diseases, Copenhagen, T. Lund, 1898; cited by Olsen.

——and Bock, cited by Olsen.

Ranson, S. W., and Billingsley, P. R.: Vasomotor Reactions from Stimulation of the Floor of the Fourth Ventricle, Am. J. Physiol. **41**:85, 1916.

——and von Hess, C. L.: The Conduction Within the Spinal Cord of the Afferent Impulses Producing Pain and the Vasomotor Reflexes, Am. J. Physiol. **38**:128, 1915.

——Kabat, H., and Magoun, H. W.: Autonomic Reactions Induced by Electrical Stimulation of the Hypothalamus, abstr., Proc. Am. Physiol. Soc., 1934, p. 85.

Raymond, cited by Mirallié.

Raymond, M. P.: Des ephidroses de la face, Arch. de neurol. **15**:51 and 212, 1888.

Rimbaud, cited by Mirallié.

Rossolimo, G.: Zur Symptomatologie und chirurgischen Behandlung einer eigenthümlichen Grosshirncyste, Deutsche Ztschr. f. Nervenh. **6**:76, 1895.

Rotky, H., and Klein, O.: Studien über Venendruck, Kapillarströmungsdruck und Arteriendruck bei Hemiplegikern, Wien. Arch. f. inn. Med. **10**:585, 1925.

Schäfer, E. A.: The Cerebral Cortex, in Schäfer, E. A.: Textbook of Physiology, London, Y. J. Pentland, 1900, vol. 2, p. 697.

Schrottenbach, H.: Beiträge zur Kenntnis der Uebertragung vasovegetativer Funktionen in Zwischenhirn, Ztschr. f. d. ges. Neurol. u. Psychiat. **23**:431, 1914.

Schüller, M.: Die chirurgische Klinik zu Greifswald im Jahre 1876: I. Krankheiten des Kopfes, Deutsche Ztschr. f. Chir. **9**:228, 1878.

Scott, J. M. D., and Roberts, F.: Localization of the Vasomotor Centre, J. Physiol. **58**:168, 1923.

Seeligmüller, cited by Bikeles and Gerstmann.

Sherrington, C. S.: The Integrative Action of the Nervous System, New Haven, Conn., Yale University Press, 1906, p. 241.

Sicard and Guillain, cited by Mirallié; also by Villaret and Jonesco.

Tixier, cited by Mirallié; also by Villaret and Jonesco.

Villard, cited by Villaret and Jonesco.

Villaret, M., and Jonesco, D.: Les modifications de la pression veineuse au cours des hémiplégies organiques et des séquelles des traumatismes cranio-cérébraux, Presse méd. **34**:1265, 1926.

——and Théodoresco: Ann. de méd. **13**:189, 1923; cited by Villaret and Jonesco.

Wang, G. H., and Richter, C. P.: Action Currents from the Pad of the Cat's Foot Produced by Stimulation of the Tuber Cinereum, Chinese J. Physiol. **2**: 279, 1928.

Woodworth, R. S., and Sherrington, C. S.: A Pseudo-Affective Reflex and Its Spinal Path, J. Physiol. **31**:234, 1904.

Zenner, P., and Kramer, S. P.: Operation for Brain Tumor, with the Occurrence of Hitherto Unrecognized Circulation Phenomena, New York M. J. **90**:651, 1909.

THE CENTRAL NERVOUS SYSTEM IN MUSHROOM POISONING

REPORT OF TWO CASES WITH TOXIC ENCEPHALITIS

ELI MARCOVITZ, M.D.
AND
BERNARD J. ALPERS, M.D.
PHILADELPHIA

Little attention has been given to the central nervous system in reports of mushroom poisoning, and the literature contains few neuropathologic studies. The object of this paper is to review the neurologic manifestations and the neuropathologic observations hitherto reported and to present studies of the brain and the spinal cord in two cases.

REVIEW OF CLINICAL FINDINGS

Manifestations of involvement of the central nervous system have frequently been mentioned in reports of mushroom poisoning.

Ford [1] mentioned coma, cyanosis, a fall in temperature, convulsions and ocular symptoms. Six cases with one death were reported by Schürer.[2] In the fatal case the eyes were fixed upward and to the left; there were clonic convulsions and then somnolence and coma, followed by death. Clark, Marshall and Rowntree [3] noted vasomotor collapse, delirium, confusion, exaggerated reflexes, with a bilateral Babinski sign, rigidity and tremors and a temperature subnormal at first, later rising to 107 F. A case with a remission for nine days was described by Gautier and Saloz.[4] There were prostration, cyanosis and miosis. Following the remission the patient became prostrated and apathetic, with sluggish pupils, loss of reflexes and an irregular, weak pulse. Blank [5] observed confusion, somnolence, bilateral paralysis of the abducens nerve, anisocoria, miosis,

---

From the Laboratory of Neuropathology in the Institute of the Pennsylvania Hospital and from the Medical Wards of Dr. Thomas McCrae and Dr. Arthur Newlin in the Pennsylvania Hospital.

1. Ford, W. W.: The Toxins and Antitoxins of Poisonous Mushrooms (Amanita phalloides). J. Infect. Dis. **3**:191, 1906

2. Schürer, J.: Kasuistischer Beitrag zur Kenntnis der Pilzervergiftungen, Deutsche med. Wchnschr. **38**:548, 1912.

3. Clark, M.; Marshall, E. K., and Rowntree, L. G.: Mushroom Poisoning, J. A. M. A. **64**:1230 (April 10) 1915.

4. Gautier, P., and Saloz, C.: Remission et survie prolongée dans un cas mortel d'empoisonnement par "l'amanite phalloide," Rev. méd. de la Suisse Rom. **37**:291, 1917.

5. Blank, G.: Ueber Knollenblätterpilzvergiftung, München. med. Wchnschr. **67**:1032, 1920.

ptosis, hypotonus of the extremities, areflexia and incontinence. Poisoning of a family of four was reported by Treupel and Rehorn.[6] Three of the patients recovered without having shown any symptoms referable to the nervous system, while the fourth died after delirium. Murphy[7] described two patients with blurred vision, sweating, a low temperature and a rapid pulse, who recovered after emesis and the administration of atropine. These patients were probably poisoned by Amanita muscaria rather than by Amanita phalloides, since in cases due to the former atropine acts as a specific antidote. Welsmann[8] mentioned a case in which the left achilles reflex and both patellar reflexes were absent and there was a positive Babinski sign on the right, and another case with a bilateral Babinski sign. As general neurologic signs he mentioned somnolence, exaggerated reflexes, which later might be lost, pains, convulsions and stiffness of the neck. He also stressed the occurrence of circulatory weakness in the fatal cases, postulating that it was due to paralysis of the vasomotor centers in the brain, and maintaining that the prognosis in any particular case was favorable as long as no signs of circulatory failure occurred. Steinbrinck and Münch[9] divided the nervous symptoms into: (1) central, with the occurrence of somnolence, spasms and convulsions, catatonic reactions, blindness, sensory disturbances, paralysis of the bladder and spasm of the sphincter, and (2) peripheral, with sensory changes, weakness and paralysis of the extremities. The former group were thought to be due to changes in the brain caused by severe damage to the liver, in accordance with Kirschbaum's work, and the latter, to be due partly to toxic neuritis and partly to fatty changes in voluntary muscle. Seven fatal cases were reported by Silberbauer and Mirvish,[10] in which there occurred coma, spasticity, Babinski responses, rigidity, twitchings of the limbs and violent movements. Stahr,[11] in two fatal cases, noted convulsions, opisthotonos and a rise of temperature to 41.8 C. (107.2 F.) in one, and disorientation in the other.

Summary.—Not all cases of mushroom poisoning present evidences of involvement of the central nervous system, but in the cases that do, the most common neurologic manifestations are those indicating generalized cerebral involvement, for example, prostration, confusion, delirium, convulsions, somnolence and coma. In addition, a number of rather heterogeneous signs have been recorded indicating widespread involvement of the nervous system. Visual disturbances, such as amblyopia and rarely blindness, pupillary disorders, such as miosis, anisocoria and sluggish reactions, and ocular palsies occur. Involuntary

---

6. Treupel, G., and Rehorn, E.: Ueber Knollenblätterschwamm Vergiftung, Deutsche med. Wchnschr. **46**:509, 1920.

7. Murphy, F. J.: Two Cases of Mushroom Poisoning, Brit. M. J. **2**:165, 1924.

8. Welsmann, L.: Vergiftung mit Amanita Phalloides, Deutsches Arch. f. klin. Med. **145**:151 (Oct.) 1924.

9. Steinbrinck, W., and Münch, H.: Ueber Knollenblätterschwammvergiftung, Ztschr. f. klin. Med. **103**:108, 1926.

10. Silberbauer, S. F., and Mirvish, L.: Notes on Cases of Fungus Poisoning, J. M. A. South Africa **1**:549 (Nov. 12) 1927.

11. Stahr, H.: Ueber tödliche Lorchelvergiftungen, Deutsche med. Wchnschr. **56**:1993, 1930.

movements, such as tremors and twitchings, increased or decreased tonus with weakness or paralysis of the extremities, and loss or exaggeration of reflexes with a Babinski sign, may be found. Incontinence, paralysis of the bladder and spasm of the sphincter are sometimes observed. Meningeal signs, such as stiffness of the neck and opisthotonos, occur. Finally, there is vasomotor collapse, with cyanosis, a fall in blood pressure, sweating and a rapid, weak, irregular pulse.

There seems to be no consistent relationship in the appearance of these signs, or in their combinations, and no definite nervous symptomatology can be outlined. In any particular case almost any of the signs may appear, singly or in combination, depending on the degree and extent of generalized and focalized involvement of the nervous system.

NEUROPATHOLOGIC FINDINGS

In spite of the general recognition of involvement of the central nervous system in mushroom poisoning, there have been comparatively few adequate neuropathologic studies in cases which have come to necropsy. Many authors have reported in detail changes in other organs but have omitted even a gross description of the brain and the spinal cord.

Gross examinations of the brain and cord have revealed little. Blank,[5] and Silberbauer and Mirvish[10] in the third of their fatal cases, reported that nothing pathologic was found in the brain. The presence of hyperemia alone was mentioned by Plowright[12] and by Steinbrinck and Münch[9] in the second of their two cases. "Important brain softenings" were found by Hegi.[13] Small hemorrhages have been observed by Ford[1] in the brain and cord, by Kratzeisen[14] in the cerebral substance, by Steinbrinck and Münch[9] in the pons, and by Silberbauer and Mirvish[10] under the ependyma of the ventricles in their first case. In this case the authors noted also cerebral edema. Schnyder[15] had previously pointed out the presence of cerebral edema as the only constant and important finding in the nervous system in a series of four cases, and had suggested this factor as a possible differentiating feature between mushroom and phosphorus poisoning.

The earliest detailed microscopic study of the brain in mushroom poisoning was published by Schürer in 1912.[2] The case was that of a child, aged 5 years, who presented the only fatality in a family of six, all of whom were stricken. The clinical neurologic picture has already been outlined. Grossly there was pial congestion. Microscopic examination revealed changes in the nerve cells, the neuroglia and the adventitial cells of the blood vessels. The nerve cells

12. Plowright, C.: Remarks on Poisoning by Fungi (Amanita phalloides), Brit. M. J. **2**:541, 1905.

13. Hegi, K.: Beitrag zur Lehre von dem Pilzervergiftungen, Deutsches Arch. f. klin. Med. **65**:385, 1910.

14. Kratzeisen, E.: Zwei Fälle von Pilzervergiftung, Wien. klin. Wchnschr. **38**:96, 1925.

15. Schnyder, K.: Ueber Hirnödem bei Pilzervergiftungen, Vrtljschr. f. gerichtl. Med. **54**:211, 1917.

stained lightly. There were vacuolated nuclei and small nuclei with dark granules. Some processes had "incrustations," and with the Bielschowsky stain argentophilic granules were visible. The changes in the nerve cells were likened to Nissl's "severe cell disease." The neuroglia had small nuclei and cell bodies larger and rounder than normal, the changes being "like those of acute cerebral processes." The adventitial cells showed some metachromia and greenish-yellow granules. The endothelial cells were normal, and axis-cylinder preparations showed no abnormalities. Fat granules were found in the bodies and processes of nerve cells, in the neuroglia and in adventitial cells. In general the author thought that the changes were regressive rather than inflammatory.

Fatty degeneration of endothelial cells was reported by Schmidt,[16] who, contrary to Schürer's findings, declared that he had never observed in mushroom poisoning the occurrence of fat in the nerve parenchyma itself. Cloetta[17] stated generally that in mushroom poisoning there are regressive rather than inflammatory cerebral changes, which include the nerve cells as well as the neuroglia. In two cases Weimann[18] observed diffuse swelling and degeneration of the ganglion cells, some hyperplasia of glia, particularly in the cranial nerve nuclei, and also encephalitic foci in the medulla.

REPORT OF CASES[19]

CASE 1.—*Ingestion of Amanita phalloides, followed by nausea, vomiting and diarrhea, and later by jaundice, oliguria, drowsiness, blurring of vision, and pupillary and reflex disturbances. Death within five days. Necropsy revealed degenerative and inflammatory cerebral changes, destruction of parenchyma in the liver and lesser changes in the heart, kidneys, suprarenal glands and spleen.*

History.—Anna P., aged 26, was admitted to the Pennsylvania Hospital, to the service of Dr. Arthur Newlin, on Sept. 20, 1932, complaining of abdominal cramps, nausea, vomiting and diarrhea. Four days previously she had eaten mushrooms collected by her husband. Early the next morning she was seized with cramps, followed by vomiting and diarrhea. On the second day she complained of dizziness and became drowsy. The symptoms continued, with blurring of vision.

Examination.—On admission the patient was drowsy and icteric. The pupils were constricted and reacted slowly to light. There was tenderness on palpation of the right upper quadrant, and the liver edge was four fingerbreadths below the costal margin. The blood pressure was 80 systolic and 40 diastolic; the pulse was regular, and the rate was 152. The reflexes were not obtained without reinforcement.

Laboratory Findings.—The urine was turbid and light amber; the specific gravity was 1.018; there were: albumin (3 plus), sugar (1 plus), a few leuko-

16. Schmidt, M. B.: Pathologische Veränderungen nach Pilzvergiftungen, Ztschr. f. ang. Anat. u. Konstitutionslehre **3**:146, 1918.

17. Cloetta, M., in Bergmann, G., and Staehelin, R.: Handbuch der inneren Medizin, ed. 2, Berlin, Julius Springer, 1927, vol. 4, pt. 2, p. 1738.

18. Weimann, W.: Intoxikationen, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 7, p. 75.

19. A more complete clinical and general pathologic report of these cases and of mushroom poisoning has been made by Vanderveer and Farley (to be published).

cytes and a few epithelial cells. The total output of urine in the hospital was 300 cc. The blood had an icteric index of 27.8; the sugar content was 51 mg. per hundred cubic centimeters, the urea nitrogen, 33.3 mg., and the creatinine, 1.3 mg. A blood count showed 4,100,000 erythrocytes and 9,500 leukocytes, with 80 per cent polymorphonuclears, 14 per cent lymphocytes and 6 per cent monocytes. There was vacuolation of the polymorphonuclears, and giant platelets were present.

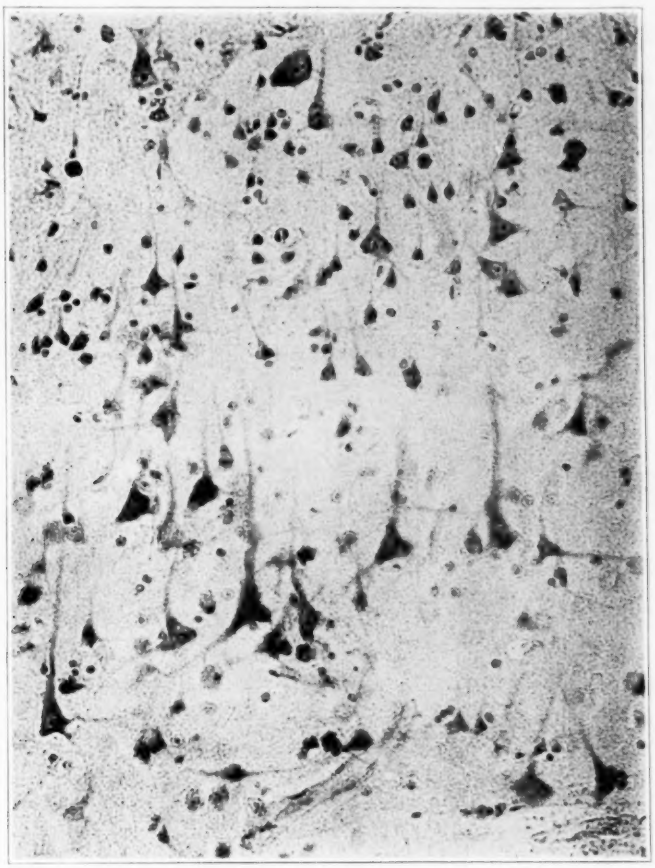


Fig. 1 (case 2).—Swelling of the cortical cells with areas of erosion in the lamina pyramidalis. Toluidine blue stain; × 149.

Course.—The pupils became fixed to light; the blood pressure fell to 60 systolic and 30 diastolic, and the patient died on the morning after admission.

Necropsy.—There were myocardial hemorrhages. The liver presented a rather uniform destruction of the parenchyma; there was a considerable amount of fat but no glycogen. In the suprarenal glands there was a moderate round cell infiltration of the medulla, with some fatty vacuolation of the cortical cells. The tubular epithelium of the kidneys was swollen and granular, but there were

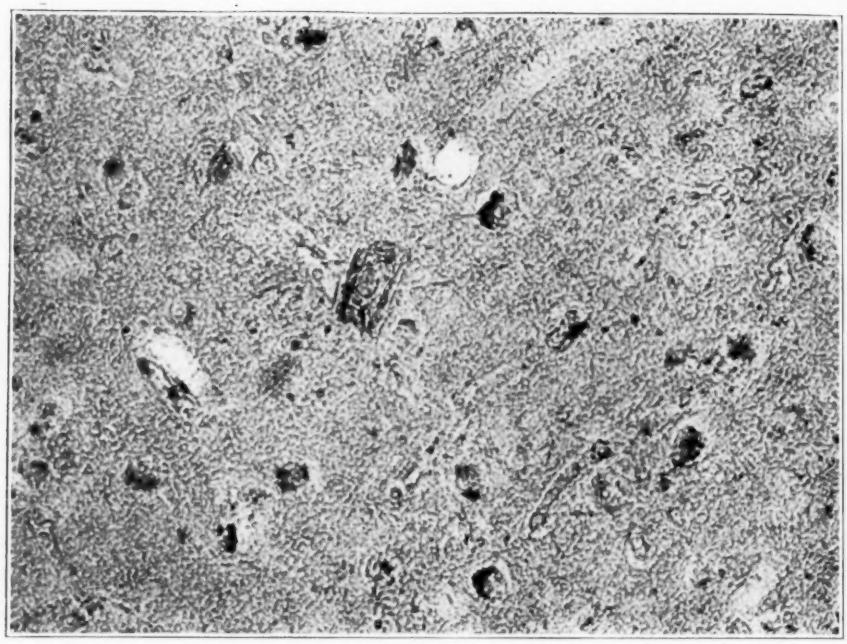


Fig. 2 (case 2).—Fatty degeneration of the cortical ganglion cells. Scarlet red stain; × 230.

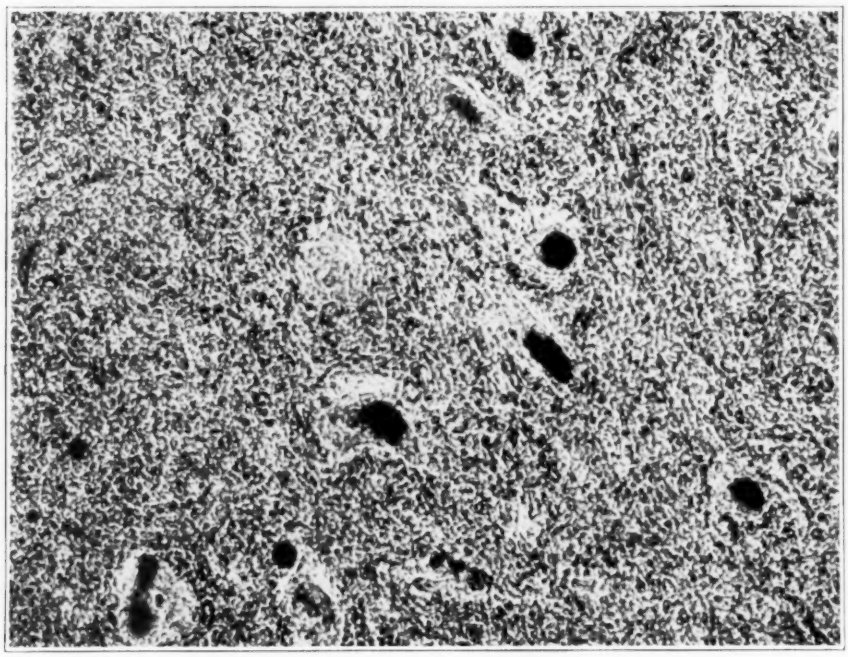


Fig. 3 (case 2).—Fatty degeneration of the ganglion cells of the hypoglossal nucleus. Scarlet red stain; × 230.

no acute changes in the glomeruli. The sinuses of the spleen were filled with blood, but the pulp spaces were collapsed, with slight infiltration by round cells and polymorphonuclears. The lungs, pancreas, stomach, intestines, pelvic organs, hypophysis, voluntary muscle and bone marrow were all normal.

Brain and Spinal Cord: Grossly the brain was edematous and congested. Scattered punctate hemorrhages were present, especially around the floor of the fourth ventricle and the midbrain. Bilaterally in the dentate nuclei of the cerebellum and in the striate regions there were bluish areas of discoloration. There was some hemorrhagic staining over the dorsal surface of the cord.

Microscopically, in places over the cortex the meninges seemed to be filled with a mass of débris, consisting of blood pigment, free red blood cells, lympho-

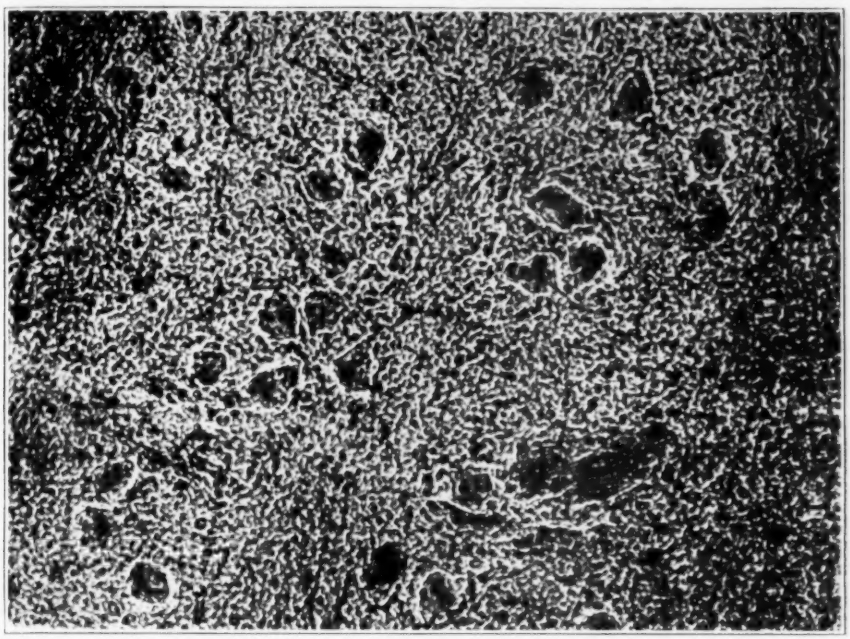


Fig. 4 (case 1).—Fatty degeneration of all the cells of the inferior olive. Scarlet red stain; × 230.

cytes and a great number of macrophages. Throughout the cortex there was a marked dropping out of ganglion cells, especially in the lamina pyramidalis. This was most obvious in the frontal and temporal areas. The ganglion cells showed toxic changes, such as swelling of the cell body, fragmentation and dissolution of the Nissl substance, vacuolation of the cytoplasm and a homogeneous, pale, swollen nucleus with a prominent nucleolus. Many shadow cells were present. On the other hand, many ganglion cells were pyknotic and stained heavily, but these also contained many small vacuoles. In the basal ganglia, hypothalamus, cerebellum and brain stem similar ganglion cell changes were present in varying degree.

In the region of the basal ganglia and around the dentate nuclei numerous vessels were full of bacteria, rods, cocci and spore-bearing forms. In the tissue

of these areas many single bacteria were dispersed, and a few colonies were visible. However, there was no evidence of an inflammatory reaction around these colonies, and only a few of the vessels which contained organisms showed a mild lymphocytic infiltration.

Throughout the brain, on the other hand, there were numerous scattered vessels containing no organisms but presenting a perivascular lymphocytic infiltration which varied from a few cells to a very thick collaring. These perivascular infiltrations were found most frequently at the borders of gray and white matter, especially in the striate regions. However, they were also found in the meninges, under the cortex, in the pallidum, in the root of the trigeminal nerve in the pons, and in the medulla. In the medulla there was also a small focus of glial reaction

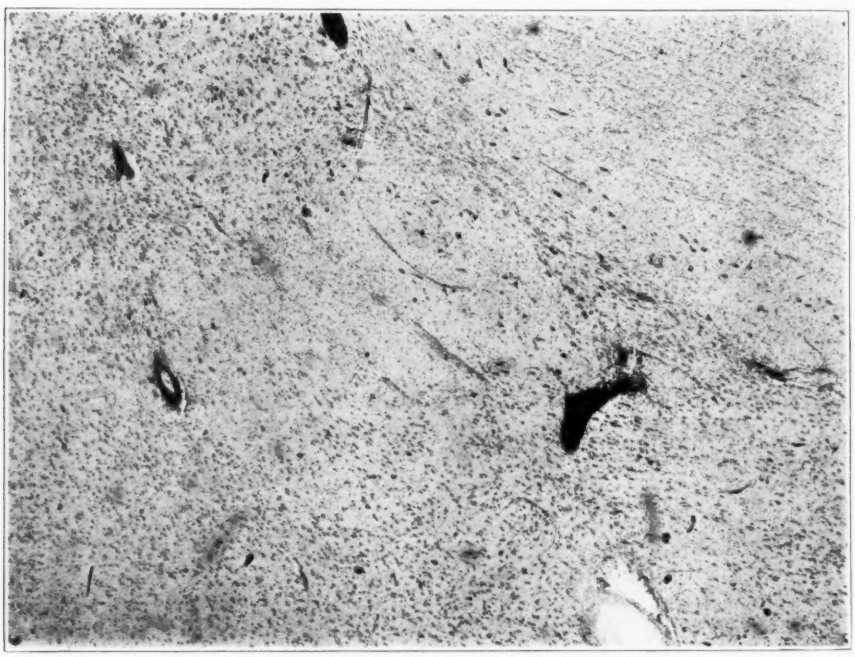


Fig. 5 (case 1).—Several foci of perivascular infiltration in the caudate and putamen, at the edge of the anterior limb of the internal capsule. Toluidine blue stain; × 44.

and proliferation, consisting mostly of altered microglia, with a few swollen astrocytes. No compound granular cells were visible anywhere in the brain.

Some of the small cortical vessels were mildly thickened or hyalinized, with some adventitial proliferation, and in some the endothelial cells were moderately swollen. In the pallidum there was a mild degree of calcium deposit in the vessels. Many small fresh hemorrhages were present in the pons under the ventricle.

Staining with scarlet red revealed the presence of fat in the ganglion cells everywhere. The cortical cells contained fine droplets of fat. Small droplets of fat were also present in the cells of the ependyma, in the neuroglia, in the microglia and in the endothelial cells. Silver stains for microglia[20] showed

20. Weil, A., and Davenport, H. A.: Staining of Oligodendroglia and Microglia in Celloidin Sections, Arch. Neurol. & Psychiat. **30**:175 (July) 1933.

changes indicative of early stages of toxic swelling, and many microglia showed fairly severe swelling of the type described by Marcovitz and Alpers,[21] with ballooning of the cell body and few processes, which were lacking in side-branches and spines and contained vacuoles and varicosities along their course. Axis-cylinder stains disclosed no abnormalities.

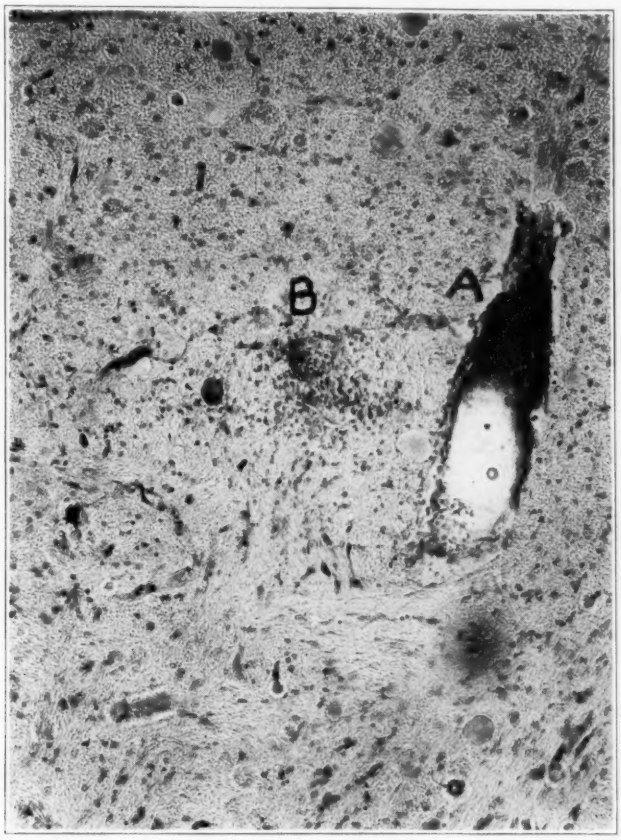


Fig. 6 (case 1).—A large perivascular inflammation (*A*) and a parenchymatous focus of glial infiltration (*B*) in the reticular substance of the medulla. Toluidine blue stain; × 115.

Summary of Neuropathologic Changes.—Grossly, the brain showed edema, congestion and scattered punctate hemorrhages. Microscopically, there were cortical areas of erosion, widespread toxic changes in the ganglion cells and toxic changes in the glial apparatus. Many bacterial forms were present in vessels and in the tissue in localized areas, with no accompanying inflammation. A well marked lymphocytic infiltration occurred around vessels in various parts of the

21. Marcovitz, E., and Alpers, B. J.: Swelling of the Microglia: Reaction to Intoxication, Arch. Neurol. & Psychiat. **31**:1045 (May) 1934.

brain, and there was an area of glial reaction and proliferation in the medulla. Many small hemorrhages were present under the floor of the fourth ventricle. Fat was present throughout the brain in the ganglion cells, neuroglia, microglia, ependymal cells and vascular endothelial cells. No changes were found in the axis-cylinders.

CASE 2.—*Ingestion of Amanita phalloides, followed by abdominal pain, nausea and vomiting, and later by oliguria, jaundice, drowsiness, confusion, pupillary disturbances, coma, involuntary movements and hyperpyrexia. Death within seven days. Necropsy revealed severe degenerative and mild inflammatory changes in the brain, liver degeneration, and changes in the heart, kidneys, suprarenal glands, spleen, lungs and bladder.*

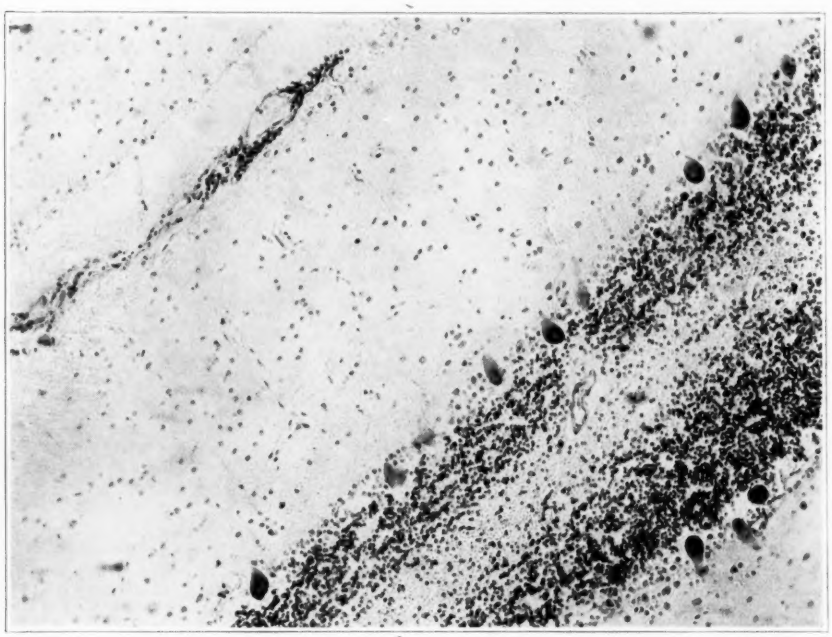


Fig. 7 (case 1).—Mild infiltration of the cerebellar meninges with lymphocytes, together with swelling and loss of cells in the Purkinje layer. Toluidine blue stain; × 115.

History.—Joseph P., aged 36, was admitted to the Pennsylvania Hospital, to the service of Dr. Thomas McCrae, on Sept. 20, 1932, complaining of abdominal pain. Four days previously he had eaten mushrooms which he had gathered. Early the next morning he was awakened by severe abdominal pain, followed by vomiting and persistent nausea. There was no diarrhea; the urinary output was scanty.

Examination.—On admission the temperature was 99.3 F., the pulse rate was 122, the respiratory rate was 24 and the blood pressure was 85 systolic and 56 diastolic. The patient was icteric and drowsy; the pupils were normal, and liver dulness extended 8 cm. below the costal margin. Neurologic examination gave negative results.

Laboratory Findings.—The urine contained from 8 to 10 leukocytes per low power field and granular and hyaline casts. A blood count showed: hemoglobin, 95 per cent; erythrocytes, 4,300,000; leukocytes, 4,950, and polymorphonuclears, 85 per cent. The urea nitrogen of the blood was 42.4 mg. per hundred cubic centimeters; the creatinine, 1.5 mg., and the icteric index, 33.5.

Course.—On the day after admission the patient was jaundiced and confused; the pupils were contracted. On the second day the blood sugar was 104 mg. per hundred cubic centimeters; the urea nitrogen, 21.7 mg., and the creatinine, 1.3 mg. On the third day, the urine contained sugar (2 plus), bile (2 plus) and granular casts. The patient was comatose, and his hands became puffed and

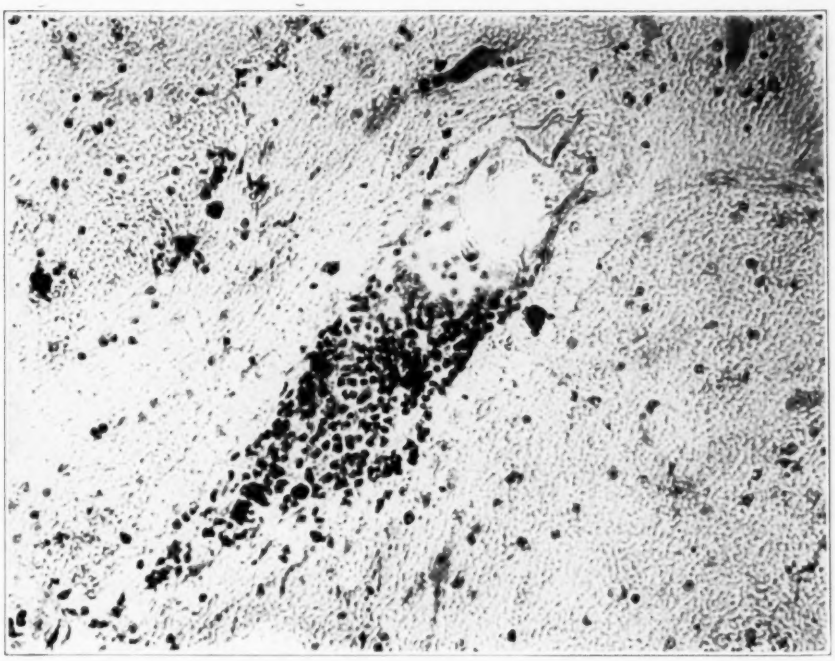


Fig. 8.—One of the few areas of perivascular infiltration in case 2. The area is in the pallidum. Toluidine blue stain, × 179.

shiny. The pupils were dilated and reacted sluggishly to light. The pulse rate was 154. Terminally, there appeared slow upward movements of the forearms and a plum-colored flush of the neck, and the temperature rose to 106 F.

Necropsy.—There were myocardial hemorrhages and pulmonary edema. In the spleen there was swelling of the intimal lining of the arterioles of the malpighian centers. The liver showed fatty degeneration and hemorrhages. The cortical cells of the suprarenals were vacuolated. In the kidneys the tubular epithelium was swollen and granular, and hemorrhages were present beneath the pelvic epithelium. The bladder contained hemorrhages into the mucosa and muscle. The stomach, intestines, pancreas, aorta, voluntary muscle, bone marrow and hypophysis were normal.

Brain and Cord: Grossly, the brain was edematous and congested. Otherwise there was nothing abnormal grossly in the brain or cord.

Microscopically, the meninges were edematous and somewhat thickened in places and contained some macrophages and lymphocytes. Changes in the cortex were universal. Loss of cells was present everywhere and in all layers; it was especially marked in the lamina pyramidalis in the frontal and temporal regions, where the architecture was markedly disturbed. The ganglion cells had undergone severe changes. The cell bodies and processes were markedly swollen; the cytoplasm was vacuolated and pale, containing almost no Nissl substance. The nuclei were swollen and metachromatic, with prominent nucleoli. Neuronophagia was prominent in some parts of the cortex. The Betz cells were not so severely

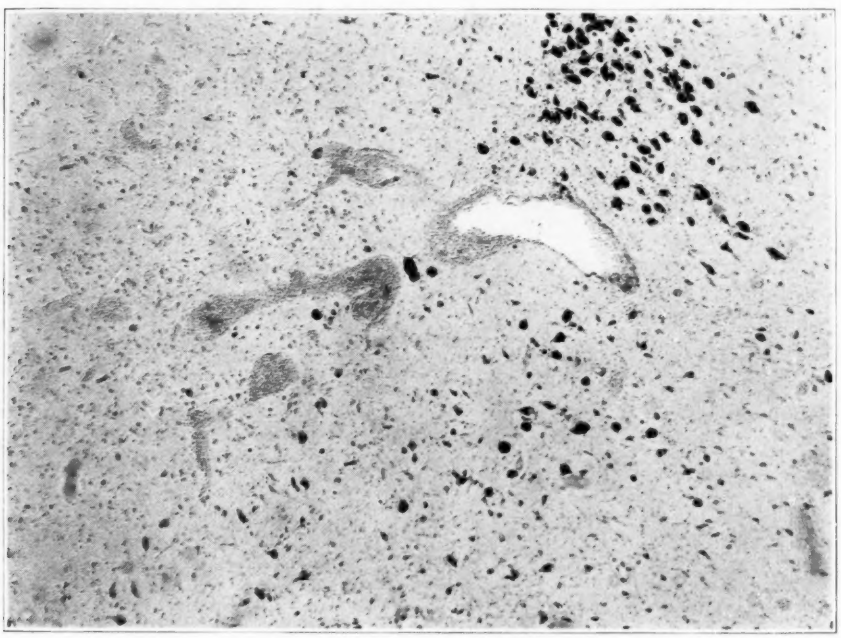


Fig. 9 (case 1).—Extensive punctate hemorrhages under the ependyma in the pons near the locus caeruleus. Toluidine blue stain; × 138.

injured, but they also showed some fragmentation of the Nissl material. In the striatum the small cells were more markedly changed than the large cells. The cells of the hypothalamus, cerebellum and brain stem also were affected, but not so severely or universally. The large motor cells in the brain and cord seemed to be the least affected. However, many cells in the anterior horns showed a peculiar vacuolation.

In various parts of the brain were small vessels with from mild to moderate degrees of perivascular lymphocytic infiltration. These were present in the cortex of the uncus, in the meninges of that region, under the ependyma of a lateral ventricle, on the border between the pallidum and the anterior commissure, in the region of the substantia ferruginea in the pons, in the inferior cerebellar peduncle and in small numbers in the subcortical white matter. The small vessels

throughout the cortex were prominent, with a mild adventitial proliferation. A greenish pigment was present in the perivascular spaces of many vessels and scattered through the tissue of the pallidum. The vessels of the pallidum showed some calcium deposit.

With scarlet red fat was visible everywhere, as in case 1, but was even more abundant. It was contained in the ependymal cells, the endothelial cells, the neuroglia and the microglia, and in the ganglion cells everywhere except in the substantia nigra. Staining for microglia showed various stages of toxic swelling, as in case 1. No abnormalities were seen in the axis-cylinders.

Summary of Neuropathologic Changes.—Grossly the brain presented edema and congestion. Microscopically there were severe widespread toxic disease of the ganglion cells and areas of erosion in the cortex. The glial apparatus showed toxic changes. A mild to moderate degree of perivascular lymphocytic infiltration and adventitial proliferation occurred in various parts of the brain. Fat was present throughout the brain, in the ganglion cells, neuroglia, microglia, ependyma and endothelium. The axis-cylinders were normal.

COMMENT ON PATHOLOGIC CHANGES

The changes were essentially similar in the two cases. There was marked cerebral edema. The meninges were edematous and mildly infiltrated. There was widespread toxic disease of the ganglion cells, with cortical areas of cell loss. This process affected in various degrees the ganglion cells in all parts of the brain but was most marked in the cortex. The glial apparatus showed toxic changes. On the other hand, the endothelium was not markedly swollen or proliferated. Fat was present in varying degree in practically all cell elements throughout the brain, including the ganglion cells, neuroglia, microglia, ependyma and endothelium. Case 2 showed greater toxic change, seen in the greater degree of cell change and in the greater abundance of fat within the cells.

Both these cases, in addition to the usual toxic regressive changes, which might be expected, showed evidence of inflammation, with the presence of alterative, proliferative and infiltrative changes. The bacteria present in case 1 can be disregarded as a complicating factor. They have been identified morphologically as types of nonpathogenic saprophytes. Furthermore, they were localized in areas which showed postmortem discoloration, and very few of the bacterial foci showed evidence of inflammatory reaction in their vicinity. Even in the very few instances in which bacteria were present in vessels with perivascular infiltration, the infiltration consisted entirely of lymphocytes, without a single polymorphonuclear cell to point toward an acute bacterial process. Furthermore, such saprophytic invasions are not rare in cases in which death occurs during hot weather. In case 2, which presented essentially the same pathologic picture, no organisms were found.

It is significant that the foci of perivascular infiltration bore no relation to the areas of greatest cell destruction and that no gitter cells were present in either case. Ganglion cell changes were more marked in case 2 than in case 1, but the inflammatory reaction was less and there were no hemorrhages. No cortical foci of inflammation were found in case 1, and in case 2 there was only one focus in the uncus, a region where the ganglion cell changes were not as marked as in other areas of the cortex. Furthermore, the parenchymatous focus of glial change and proliferation in the medulla in case 1 also serves to indicate the presence in these cases of an inflammatory process of a nonsuppurative type, which is histologically difficult to distinguish from a primary infectious inflammatory disease.

The finding of such universal involvement of all the elements in the nervous system in these cases of mushroom poisoning readily explains the widespread and varying clinical neurologic manifestations that occur in this intoxication.

Except for the evidences of inflammation which were present in both these cases, the pathologic changes might be classified simply as those of a toxic encephalopathy.

Previous investigators have stressed the regressive nature of the changes in the brain in mushroom poisoning (Schürer,[2] Schmidt[16] and Cloetta[17]). Schmidt was unable to corroborate Schürer's observation of fat in the nerve parenchyma, whereas the cases presented here showed the presence of fat in practically all elements throughout the brain.

It has been repeatedly observed by various authors that the reaction of the central nervous system to toxins, whether endogenous or exogenous, is in the form of what has been called "toxic encephalitis" or "encephalopathy," in which the changes are entirely of a regressive nature, and in which infiltration with mesodermal elements is not present (Kirschbaum,[22] Grinker and Stone,[23] Winkelman and Eckel,[24] Low[25] and Globus[26]). However, a modification of this conception

22. Kirschbaum, W.: Ueber den Einfluss schwerer Leberschädigungen auf das Zentralnervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **88**:487, 1924.

23. Grinker, R. R., and Stone, T. T.: Acute Toxic Encephalitis in Childhood, Arch. Neurol. & Psychiat. **20**:244 (Aug.) 1925.

24. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929.

25. Low, A. A.: Acute Toxic (Non-Suppurative) Encephalitis in Children, Arch. Neurol. & Psychiat. **23**:696 (April) 1930.

26. Globus, J. H.: Inflammatory Disease of the Central Nervous System, Arch. Neurol. & Psychiat. **28**:810 (Oct.) 1932.

seems to be indicated in view of the observations in the cases reported here and of reports of experimental investigations of changes in the brain following intoxications due to guanidine, experimental damage of the liver, and meat-poisoning after an Eck fistula. Pollak [27] found a diffuse, inflammatory, nonsuppurative encephalomyelitis in the brain of the cat with guanidine poisoning and of the dog with an Eck fistula studied by Fuchs.[28] The authors thought that the processes were similar and that the dog had presented the picture of endogenous guanidine poisoning owing to failure of the liver to detoxify meat derivatives.

In his studies of changes in the brain following various forms of experimental damage of the liver, Kirschbaum [22] found an inflammatory process in only one of his four dogs with an Eck fistula, none of which had shown any clinical symptoms. He believed that the metabolic disturbance had probably activated the virus of distemper, producing the inflammation. In his other animals with various forms of damage of the liver he found regressive changes occurring throughout the brain, with a predilection for the cortex rather than for the striatum. Kleinschmidt [29] studied the brains of twenty-two dogs with Eck fistulas which presented clinical signs of meat poisoning, such as ataxia, blindness, excitement and disturbances of motility and sensation. He found no evidence of inflammation in any of them, and subdural injection of an emulsion of the brains of these dogs into guinea-pigs, rabbits and one other dog produced no signs of illness.

In a recent publication, Baló and Korpássy [30] reported that six of eight dogs with Eck fistulas on a meat diet presented cerebral manifestations. Three of these showed no inflammatory changes. Of the other three, two showed perivascular round cell infiltration limited to the caudate region, and one showed a mild diffuse meningeal infiltration and a mild perivascular infiltration through the cortex. The authors made intracerebral injections of emulsions of the brains of these animals into other dogs and rabbits without producing encephalitis. They concluded that the metabolic disorders following an Eck fistula and meat feeding bring about a nonsuppurative encephalitis localized in the striate region, that the noxious agent has an elective affinity for the

27. Pollak, E.: Ueber experimentelle Encephalitis, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **23**:1, 1921.

28. Fuchs, A.: Experimentelle Encephalitis, Wien. med. Wchnschr. **71**:709, 1921.

29. Kleinschmidt, K.: Zur Frage der Encephalitis bei Hunden mit Eckscher Fistel, Ztschr. f. d. ges. exper. Med. **54**: 20, 1927.

30. Baló, J., and Korpássy, B.: The Encephalitis of Dogs with Eck's Fistula Fed on Meat, Arch. Path. **13**:80 (Jan.) 1932.

striate body and that the encephalitis is not caused by invasion with a virus. On the other hand, Crandall and Weil,[31] following damage of the liver after ligation of the common bile duct or the pancreatic duct of dogs, found necrotic, degenerative changes in the brain, with glial proliferation but with absence of mesenchymal participation in the disease process.

It seems, therefore, that there is some evidence that toxins per se may produce inflammatory changes, despite Globus'[26] assertion to the contrary. Jakob[32] mentioned Lotmar's work with dysentery toxin, in which he produced cerebral changes varying from severe necrobiotic foci to well developed inflammatory foci, with infiltrative and exudative phenomena. Some of his cases showed varying degrees and combinations of these extreme processes. The findings of Fuchs,[28] Pollak[27] and Baló and Korpássy[30] are not to be lightly dismissed by postulating the presence of some hypothetic virus, especially since the last mentioned investigators were unable to transmit the encephalitis to other animals. Furthermore, Weimann,[18] without going into greater detail, mentioned the occurrence of "encephalitic foci in the medulla" in a case of mushroom poisoning.

The two cases of mushroom poisoning presented in this paper serve as further evidence that toxins are capable of producing, in the central nervous system, an inflammation which it is often impossible to differentiate histologically from an infectious nonsuppurative encephalitis.

It might be argued that this toxic inflammation differs in no essential from the secondary inflammatory reaction. However, the usual conception of a true secondary inflammatory reaction is limited to that which occurs in the vicinity of a large necrobiotic focus, such as necrotic tissue around tumors, softenings, aseptic traumatic lesions and the pallidal necroses after carbon monoxide poisoning (Jakob[32]). Globus[27] stated: "In such instances the gross lesions provoking such inflammatory reaction are easily recognized, and the restricted character of the reaction is also indicative of the secondary character of such reactions." But the inflammations occurring in the two cases presented, as well as those found in the experimental work discussed, are distinctly not conformable to the definition just quoted. First, there were no gross necrobiotic foci to which the inflammation could be considered a reaction; second, the inflammation, instead of being restricted in character, was diffuse. Furthermore, as already pointed out, the

31. Crandall, L. A., and Weil, A.: Pathology of Central Nervous System in Diseases of the Liver, Arch. Neurol. & Psychiat. **29**:1066 (May) 1933.

32. Jakob, A.: Anatomie und Histologie des Grosshirns, Leipzig, Franz Deuticke, 1927, p. 423.

inflammatory foci observed in our cases bore no relationship to the areas or to the degree of severity of the parenchymatous degeneration.

This being the case, the question arises whether this process might not be considered a primary rather than a secondary inflammation. If inflammation is defined merely as the immediate protective and defensive reaction of tissues to injury,[33] the question becomes superfluous, since in the last analysis even the reactive inflammation around a softening would conform to this definition, and there would be no essential distinction between "primary" and "secondary" inflammation. However, most neuropathologists agree on the necessity for differentiating these processes.

A basis for the substantiation of this conception of a fundamental difference is found in the work of Opie,[34] who concluded that "inflammation is a process by means of which cells and serum accumulate about an injurious substance and tend to remove or destroy it." On the basis of this definition, a "secondary" inflammation might be defined as one which is a reaction to an injurious substance entirely derived from the necrosis of tissue.

Micro-organisms are by no means the only substances which call forth a primary inflammation. To quote Opie further: "An immense number of sterile substances, both fluid and solid, soluble and insoluble, organic and inorganic, incite a reaction which differs in no essential respect from that which follows the invasion of micro-organisms." Primary inflammations of toxic origin are therefore well recognized in general pathology.

However, owing to its bony and membraneous coverings, the hematoencephalic barrier and the quickly reacting glial apparatus, the central nervous system has much greater protection against injurious agents than has the rest of the body. The reaction of neuroglia or microglia may at times be the only indication of a toxic process (Penfield and Cone,[35] Alpers,[36] Marcovitz and Alpers [21]). But true toxic inflammations of the meninges are not unknown. Freeman [37] mentioned their production by the injection of serum, drugs or air into the subarachnoid space. Furthermore, in discussing intoxication of the nervous system

33. MacCallum, W. G.: A Text-Book of Pathology, ed. 3, Philadelphia, W. B. Saunders Company, 1925, p. 134.

34. Opie, E. L.: Inflammation, Arch. Int. Med. **5**:541 (June) 1910.

35. Penfield, W., and Cone, W.: Acute Swelling of Oligodendroglia, Arch. Neurol. & Psychiat. **16**:131 (Aug.) 1926.

36. Alpers, B. J.: The Reaction of the Central Nervous System to Experimental Urea Intoxication, Arch. Neurol. & Psychiat. **24**:492 (Sept.) 1930.

37. Freeman, W.: Neuropathology, The Anatomical Foundation of Nervous Disease, Philadelphia, W. B. Saunders Company, 1933, p. 117.

from a distant diphtheritic process, Weil [38] wrote: *"Besides inflammatory meningitis and encephalitis,* severe degenerative changes of nuclei in the central nervous system have been reported" (italics ours).

De la Rivière [39] showed that the toxins of Amanita phalloides have a definite affinity for the central nervous system. This investigator injected an extract of Amanita into animals and produced signs of involvement of the central nervous system. Subsequently he produced a similar but less severe intoxication in a second series of animals by injecting an emulsion made from the brains and cords of animals in his first series.

In these cases of mushroom poisoning, then, there was a toxic substance with an affinity for the nervous system which produced injury and a glial reaction and at the same time called forth an inflammatory reaction which gave no evidence of being secondary to necrosis of tissue. On this basis it seems justifiable to classify the inflammation as a primary nonsuppurative inflammatory process of toxic origin.

It is true that toxic inflammation in the central nervous system is comparatively uncommon. The conditions in which it sometimes occurs are usually characterized by purely regressive changes. As yet the factors which call forth in addition this special type of reaction are unknown. It appears, notwithstanding the conclusion of Baló and Korpássy,[30] that damage of the liver alone is not sufficient, even though it is usually present, as in the cases here reported. The three cases of Baló and Korpássy in which there was no inflammation, together with the work of Kirschbaum,[22] Kleinschmidt [29] and Crandall and Weil,[31] in which there was also no inflammation, give ample proof that for the production of a toxic encephalitis, some other factor or factors are essential. Some authors still insist on the presence or activation of some virus as the explanation for this phenomenon. However, until the existence of such a factor is definitely proved this theory must remain merely a postulate.

SUMMARY

The clinical neurologic manifestations of mushroom poisoning, as described in the literature, are reviewed and summarized.

The neuropathologic changes hitherto reported are reviewed.

Two fatal cases of poisoning by Amanita phalloides are presented, with the observations at necropsy and a detailed histologic description of the central nervous system.

38. Weil, A.: A Textbook of Neuropathology, Philadelphia, Lea & Febiger, 1933, p. 189.

39. de la Rivière, D.: Action expérimentale de la toxine phallinique et centres nerveux, Compt. rend. Soc. de biol. **93**:998 (Oct.) 1925.

In both cases a nonsuppurative inflammation was associated with, but probably not due to, a toxic-degenerative process affecting nerve cells and glia, with the presence of fat in practically all the cerebral cell elements.

The problem of toxic inflammation in the nervous system is discussed, with special reference to the changes following experimental damage of the liver.

The conclusion is reached that occasionally in some undoubtedly severe intoxications there occurs an inflammation which does not correspond with the picture of a secondary inflammatory reaction and which should be classified as a primary nonsuppurative inflammatory process.

Possible factors in the production of this reaction are discussed, and the conclusion is reached that the essential factors are as yet unknown.

CEREBRAL CHANGES IN GASTRO-INTESTINAL INFECTIONS WITH TERMINAL CACHEXIA

HISTOPATHOLOGIC STUDIES ON DYSENTERY, WITH COMMENTS ON SIMILAR OBSERVATIONS IN INTESTINAL TUBERCULOSIS

LEO ALEXANDER, M.D.
BOSTON
AND
T. T. WU, M.D.
SHANGHAI, CHINA

In a recent clinical study on the symptomatic involvement of the nervous system in different forms of dysentery [1] we decided to consider one group of manifestations in the clinical neuropsychiatric picture as probably due to inflammatory processes; in this group we had especially in mind cases of myelitis and cases in which the condition clinically resembled closely the well known picture of epidemic encephalitis. Indeed, there exist cases with disorders of sleep, reflex disorders and more or less mental confusion or only dulness which, if no gastro-intestinal symptoms were present, nobody could be blamed for diagnosing as cases of encephalitis. Sometimes also in clinical cases these nervous disorders precede the gastro-intestinal symptoms, as in Tupa's [2] experiments on animals.

Another group seemed to be merely "toxic," which term refers especially to some patients with symptomatic psychotic behavior; but we emphasized that the term toxic should be subjected to analysis. In the studies of Spielmeyer [3] and Bodechtel [4] a number of "toxic" changes in the brain were shown to be primarily circulatory or vascular, and further study may resolve the concept of toxic still more into its radicals.

From the Division of Neurology, Peiping Union Medical College, Peiping, China.

1. Alexander, L., and Wu, T. T.: Symptomatic Involvement of the Nervous System in Different Forms of Dysentery, Chinese M. J. **48**:1 (Jan.) 1934.

2. Tupa, A.: Contribution à l'étude des lésions du système nerveux central, provoquées par la toxine dysentérique, Compt. rend. Soc. de biol. **92**:114, 1925.

3. Spielmeyer, W.: (*a*) Histopathologie des Nervensystems, Berlin, Julius Springer, 1922, vol. 1; (*b*) Infektion und Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:161, 1930.

4. Bodechtel, G.: (*a*) Gehirnveränderungen bei Herzkrankheiten, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:657, 1932; (*b*) Hirnveränderungen bei den verschiedenen Formen der Urämie unter Berücksichtigung ihrer Pathogenese, Deutsches Arch. f. klin. Med. **174**:541, 1933.

A third group seemed to have relation to metabolic factors, chiefly to undernutrition and avitaminosis, not only in the cases of subacute combined sclerosis and neuritis, as described by Keefer and his collaborators [5] and by Menzel [6] and others, but also in certain cases with symptomatic psychic manifestations. The condition in this group, which in its mild form appears as a certain general slowness, difficulty and unclearness in perception, with more or less marked headache, and in its fully developed form as typical Korsakoff's psychosis, with hallucinations, disorientation, amnesia, disorders of perception and areflexia, seems to be dependent on the presence of emaciation and is proportional in severity to the degree of emaciation.

Five patients whom we had an opportunity to observe recently at the same time in the same ward illustrate this fact.

Cases 1, 2 and 3—These three patients (with bacillary dysentery of undetermined type, bacillary dysentery of the Shiga type, and bacillary dysentery of the mannite-fermenting group) were all in good general condition and showed no neuropsychiatric disturbances.

Case 4.—A man, aged 20, suffering from bacillary dysentery of the Shiga type, was not much dehydrated on admission to the hospital on Oct. 13, 1933, but was weak, emaciated and undernourished and complained of headache. On examination by us on October 18 he still appeared emaciated and weak, but no longer dehydrated. He was slow in all reactions. Memory was good, as was also attention, when once fixed. But he had difficulties in perception, often repeated questions asked him and needed detailed explanations for clearly understanding a matter. Judgment was good; he answered all questions well and willingly, but after some delay. This patient recovered soon and was discharged in an improved condition on October 24.

Case 5.—A man, aged 32, suffering from bacillary dysentery of the mannite-fermenting group, who was admitted on Sept. 12, 1933, was the patient with the most severe emaciation, prostration and dehydration whom we had seen. He came to the hospital about three months after the onset of the disease. Other somatic signs of the severe stage of starvation and dehydration were: dry, dark brownish skin, desquamating at some places; xerophthalmia and night blindness for about three weeks before admission; secondary anemia; decubital ulcer of the lumbosacral region, and nutritional edema at the region of the ankles and on the dorsa of the feet. On admission the patient was drowsy, but mentally fairly clear. Eight days after admission, on September 20, the patient was observed to have become cataleptic. When his hands were passively elevated in taking off the bedcover, he still kept them elevated in the air after being uncovered. Examination later confirmed the cataleptic behavior. On September 25, a fully developed psychosis broke out. He heard hallucinatory voices shouting and talking to him

5. Keefer, C. S.; Yang, C. S., and Huang, K. K.: The Importance of Under-Nutrition in the Production of Anemia Associated with Chronic Dysentery and Tuberculosis of the Intestine, Nat. M. J. China **15**:743, 1929; Anemia Associated with Chronic Dysentery, Arch. Int. Med. **47**:436 (March) 1931.

6. Menzel, W.: Ueber zwei Fälle von Polyneuritis und funikulärer Myelose nach bazillärer Ruhr, Deutsche Ztschr. f. Nervenh. **126**:265, 1932.

from time to time, mostly the voice of a certain Dr. Li, who had taken care of him previously in another hospital. Furthermore, he refused food and suspected persons of giving him poison. He appeared negativistic, was uncooperative and did not answer questions adequately. On September 29, the dysentery became worse and the number of stools increased. The psychotic condition continued. The patient was described as being unreasonable and uncooperative. He refused medicines and treatments and suspected poison in the medicine and food. He heard voices: somebody scolded him. He became weaker. Bed sores developed in the lumbosacral region.

On October 18, we reexamined the patient. He was extremely emaciated and dehydrated. The xerophthalmia had cleared up somewhat under haliver oil with viosterol 250 D, but the corneas still appeared dry. The condition of the skin was the same. When left to himself he lay motionless on the bed. He was slow in all reactions and movements. If one spoke to him a slow smile appeared on his face and stayed for a prolonged time. After he had spoken his mouth sometimes remained open for some time. He yawned often spontaneously. He was disoriented for time, but knew the place. He denied hearing voices now, but believed in the reality of his former hallucinations and that he had heard the voice of Dr. Li scolding him or giving him advice. Since he now no longer heard Dr. Li's voice, the patient thought that his power of hearing might have decreased. He was very slow in speech. The voice was weak and monotonous, but in general distinct; occasionally only articulatory difficulties—stumbling—appeared. He was slow in understanding simple mental tests; attention, however, was good. He was markedly dull. Perception was definitely impaired: Of six spoken numbers he was able to repeat only two or three, in spite of fixed attention. Memory was deficient; he was unable to reproduce a simple calculation or a number after slight diversion of attention. The facial expression was almost immobile; only from time to time did he open or close his eyes; no other movement occurred in the face. The mouth was for the most part slightly opened. There was no sleepiness. When left alone he closed the eyes slightly, then always opened them again and did not fall asleep. The tendon reflexes were now absent in the arms and legs; Mayer's reflex was equal on the two sides. On admission the reflexes in the arms had been normal and equal; the knee jerks also were present, but were less lively on the right side. The ankle jerks were absent on admission. At examination on October 18, marked motor suggestibility was evident also as a tendency to add active to passive movements. No catalepsy, holding against or *hakeln* was present now. There were no pathologic phenomena of the toes. No sensitiveness of the peripheral nerve trunks was found. On October 19, the patient died; death was preceded by a fall of temperature to below normal. Permission for autopsy was not obtained.

The picture in this disease resembles closely Korsakoff's hallucinatory psychosis as it occurs in chronic alcoholism, even to the somatic characteristics, such as polyneuritis with areflexia and motor suggestibility. The Korsakoff's syndrome is also observed in the avitaminotic condition described as beriberi and in generalized tuberculosis (Nelken[7] and

7. Nelken, J.: Ein Fall allgemeiner Tuberkulose mit akut einsetzender Korsakowscher Psychose unaufgeklärten Ursprungs, Neurol. polska **10**:89, 1927; Zentralbl. f. d. ges. Neurol. u. Psychiat. **47**:688, 1927.

others); recently, some authors (Meyer [8] and Minot, Strauss and Cobb [9]) have considered the alcoholic disorders themselves as due chiefly to avitaminosis.

In a number of cases of dysentery emaciation plays a definitely active rôle in the production of the nervous symptoms. These cases are usually marked also by one or more other secondary symptoms of the same etiology, such as secondary anemia, xerophthalmia, xerodermia, dehydration or nutritional edema, and cachectic purpura of the skin. It is interesting to remember that Kleist [10] found in his studies of certain symptomatic psychoses that occur after various operations—the so-called postoperative psychoses—that these are caused by and dependent on the presence of exhaustion, as demonstrated by emaciation, weakness and anemia. Recently, Borrino [11] described a case of psychic disorder in an infant clinically as "infantile cerebropathia, caused by severe malnutrition." But the definition of exhaustion, as well as that of emaciation and malnutrition, should be subjected to further analysis. One step in this analysis might be anatomic studies.

Data on changes in the brain in dysentery in man are scanty, as one may see from the brief summary in Weimann's article on infections.[12] The original observations are scattered throughout the literature.

Spielmeyer,[13] in his book on histopathology, mentioned annular hemorrhages in a case of dysentery with scurvy. Scherer [14] mentioned annular hemorrhages in the white matter of the cerebellum in dysentery. Oesterlin,[15] in a study on focal glial proliferations, reported eleven cases of dysentery, all in children from a few months to 14 years of age. Macroscopically, the cases showed severe edema of the brain and

8. Meyer, A.: Zur Frage der diabetischen Nephrose und Polyneuritis, Ztschr. f. klin. Med. **122**:688, 1932; Ueber das Vorkommen von B-Avitaminose unter den hiesigen Lebensbedingungen, Schweiz. med. Wchnschr. **62**:1243, 1932.

9. Minot, G. R.; Strauss, M. B., and Cobb, S.: "Alcoholic" Polyneuritis; Dietary Deficiency as a Factor in Its Production, New England J. Med. **208**:1244, 1933.

10. Kleist, K.: Postoperative Psychosen, in Alzheimer, A., and Lewandowsky, M.: Monographie aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1916, no. 11.

11. Borrino, A.: Stati atrofici da tuberculosi e modificazioni della psiche in bambini dei primi anni, Inst. Clin. Pediatr. Univ. Sassari., Studi Sassar. **7**:271, 1929; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **56**:423, 1930.

12. Weimann, W.: Infektionen, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, p. 119.

13. Spielmeyer,[3a] p. 401, fig. 270.

14. Scherer, H. J.: Beiträge zur pathologischen Anatomie des Kleinhirns: II. Die Erkrankungen des Kleinhirnmarkes und seiner Kerne, insbesondere des Nucleus dentatus, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:337, 1932.

15. Oesterlin, E.: Ueber herdförmige Gliawucherungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **88**:325, 1924.

leptomeningeal hemorrhages. Histologic examination showed positive pictures in only one case. In this case the patient, a child aged 17 months, had suffered from measles just before the onset of the dysentery. A short time before death, which occurred five days after the appearance of the first bloody stools, the child showed motor agitation, especially in the form of movements of the head, and frequent nausea. This patient histologically showed shrublike glial proliferation in the Purkinje and molecular layers of the cerebellum. Spielmeyer,[16] in a study on infection and the nervous system, described spots of destruction of vascular origin in the white substance of the brain in one case of dysentery. Scherer [17] reported lobular atrophy in the cerebellum in two cases of dysentery, but no glial bushes.

More systematic studies of changes in the brain in dysentery have been carried out in experiments on animals than in pathologic conditions in man. By the intravenous injection of dysentery toxin in animals, paresis of the extremities can be produced as a result of necrotic and productive foci in the spinal cord (Dopter,[18] Guggisberger,[19] Karasawa,[20] Lotmar,[21] Tupa [2] and de Assis.[22] Tupa also found anatomic foci in the medulla oblongata, cerebellum, thalamus and olfactory lobe. Lotmar could determine especially the influence of difference in dose and in individual susceptibility.

A histopathologic study of dysentery in man in a larger amount of material has not been made.

In Peiping we had the opportunity to study the brains of twenty patients of different ages who died of different forms of dysentery. Besides these, a large amount of control material of patients dying of various other acute and chronic systemic diseases was at our disposal. In the following section the twenty cases of dysentery are reported.

---

16. Spielmeyer,[3b] p. 164, fig. 1.

17. Scherer, H. J.: Beiträge zur pathologischen Anatomie des Kleinhirns: I. Die lokalen Veränderungen der Kleinhirnrinde, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:559, 1931.

18. Dopter, C.: Effets experimentaux de la toxine dysenterique sur le système nerveux, Ann. Inst. Pasteur **19**:353, 1905.

19. Guggisberger: Arb. a. d. Inst. z. Erforsch. d. Infektionskrankh. in Bern [etc.], 1908, no. 1, p. 51.

20. Karasawa, M.: Die Wirkung des Dysenterietoxins auf das Zentralnervensystem, Ztschr. f. Immunitätsforsch. u. exper. Therap. **6**:390, 1910.

21. Lotmar, F.: Zur Wirkung des Dysenterietoxins auf das Zentralnervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **8**:345, 1912; Beiträge zur Histologie der akuten Encephalitis und Myelitis, sowie verwandter Prozesse, Histol. u. histopath. Arb. u. d. Grosshirnrinde **6**:247, 1913.

22. de Assis, A.: Ueber die Natur der Giftigkeit der mannitvergärenden Dysenteriebazillen, Ztschr.f.Immunitätsforsch. u. exper. Therap. **58**:343, 1928.

REPORT OF CASES OF DYSENTERY

CASE 6.—*Chronic amebic dysentery; last acute attack of ninety-two days' duration.*

Clinical History.—A Chinese man, aged 44, a soldier, had suffered frequently from diarrhea in the summer for the past ten years. He had always been well in all other respects and had had no psychic abnormalities. He became ill forty days before admission with diarrhea, which first was watery and mucous and later bloody and in which more than twenty stools occurred in twenty-four hours. On admission (Sept. 28, 1927), the patient was much emaciated and dehydrated. The eyes were deeply sunken; the skin was dry and loose, and there was a subjective sensation of cold. Respiration was shallow and rapid. The tongue presented a thin, yellow, dry coating. The conjunctivae were anemic, the scleras slightly icteric. The intercostal spaces of the thorax were deeply sunken; expansion was poor. Pitting edema was present over both ankles and anterior tibial regions. The abdominal and cremasteric reflexes were present, but sluggish; there were no other neurologic changes. The radial pulse was feeble; its rate was 140 a minute. The blood pressure was 84 systolic and 50 diastolic. The patient presented a picture of extreme dehydration. Clinical examination revealed amebic dysentery, with amebic abscess of the liver, as proved by amebas in the stools and in pus aspirated from the abscess of the liver.

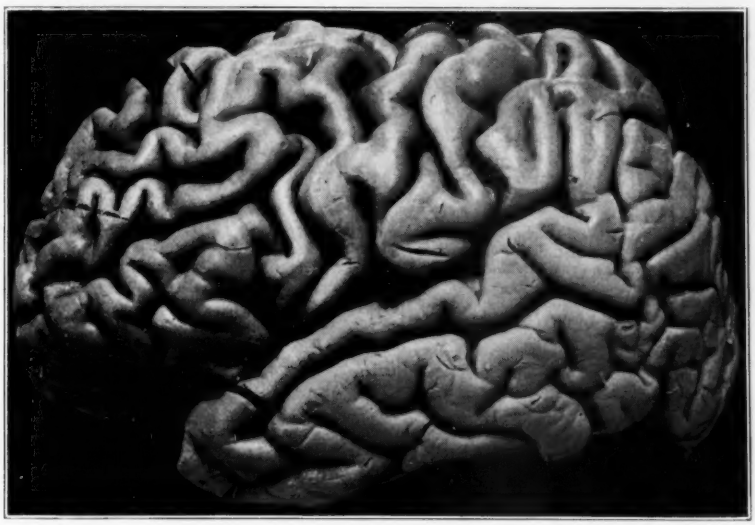


Fig. 1. (case 6).—Photograph of the left hemisphere of the brain, showing marked pseudo-atrophy of the frontal lobe.

Course.—The condition became gradually worse, and progress was more and more rapid from October 8. The extreme emaciation and dehydration and increasing anemia, which on admission was only slightly developed, were the most striking features of the pathologic picture. On October 14, a slight improvement was noted, but on October 19 the condition, especially the emaciation and dehydration, grew worse again, in spite of the fact that the frequency and character of the stools were improving. During the following days a bed sore

developed; anemia increased finally to 36 per cent hemoglobin, with 2,020,000 red blood cells, in spite of transfusion. There were transitory symptoms of peritonitis. The patient lost further weight. Congestion of the bases of the lungs developed, and fluid accumulated in the serous cavities and the subcutaneous tissue. Cachectic purpura developed on the skin of the abdomen and arms. On November 18, after an increase of fever, the temperature became subnormal. The patient died on November 19, at 7:15 p. m.; the heart stopped five minutes before the respiration.

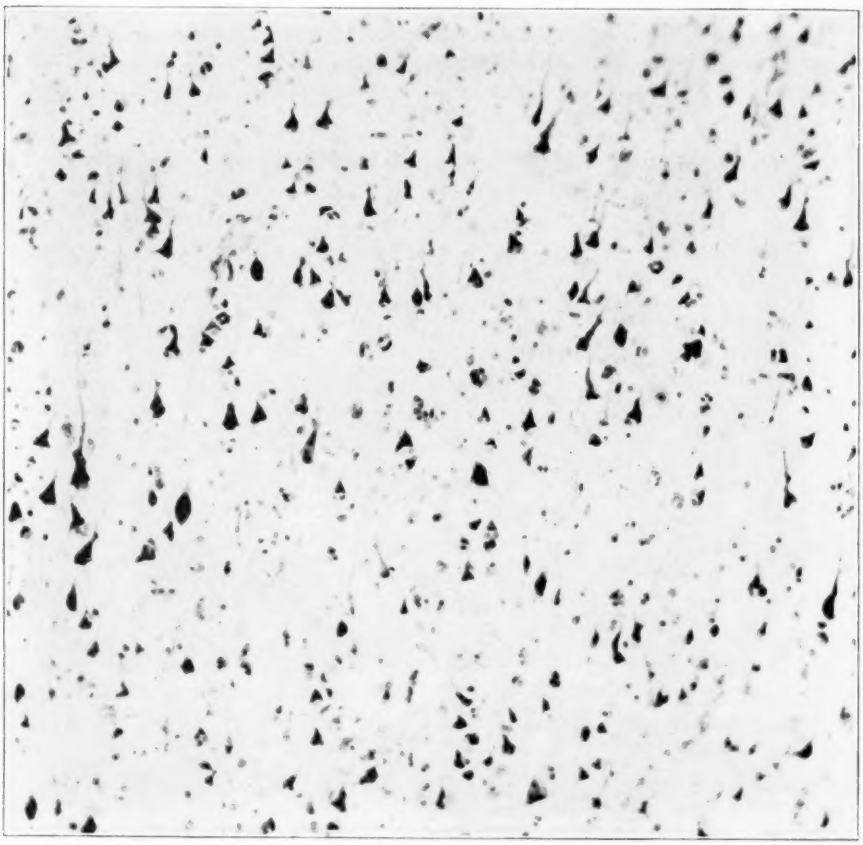


Fig. 2 (case 6).—Photomicrograph of a section from the third layer of the precentral region with the adjacent parts of the second and fourth layers. There are three confluent small early ischemic foci in the third layer. The deficiency of ganglion cells, the shadow-like ganglion cells and the glial rosettes, which are clasping ganglion cells and replacing them, in and around these foci, should be noted. Toluidine blue stain; × 155.

Autopsy.—This was performed between fifteen and nineteen hours after death. The body was greatly emaciated and measured 175 cm., weighing only 49.8 Kg.; there was a large decubitus ulcer 7 cm. in diameter over the sacral promontory; there was striking atrophy of subcutaneous fat and of pectoral and abdominal muscles, and the latter were pale and flabby.

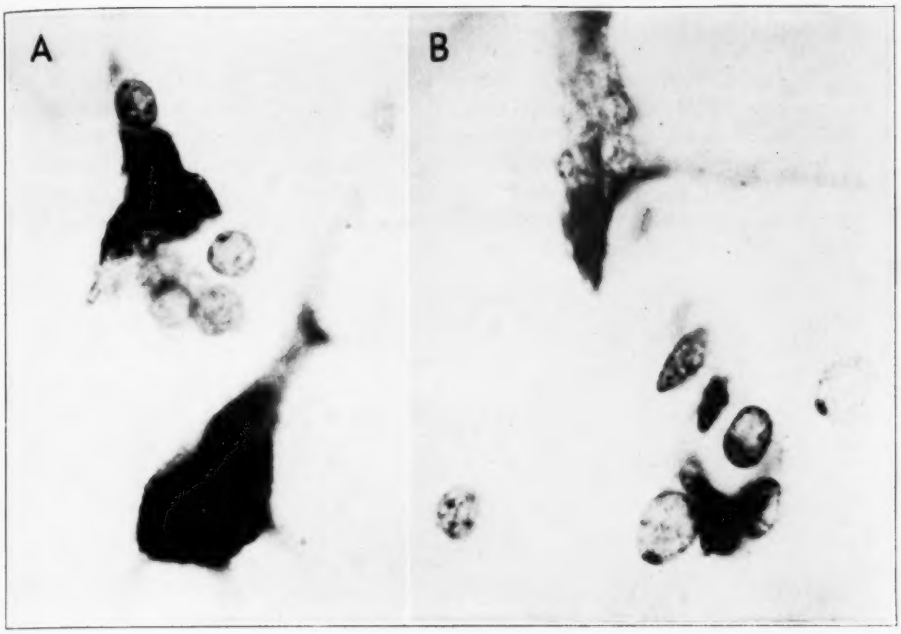


Fig. 3.—*A* (case 6), photomicrograph showing pyknomorphic ganglion cell from the third layer of the precentral region, clasped by glia cells. Toluidine blue stain; oil immersion; × 1290. *B* (case 26), photomicrograph showing pyknotic ganglion cell from the fifth layer of the frontal cortex, clasped by glial rod and round cells. Toluidine blue stain; oil immersion; × 1290.

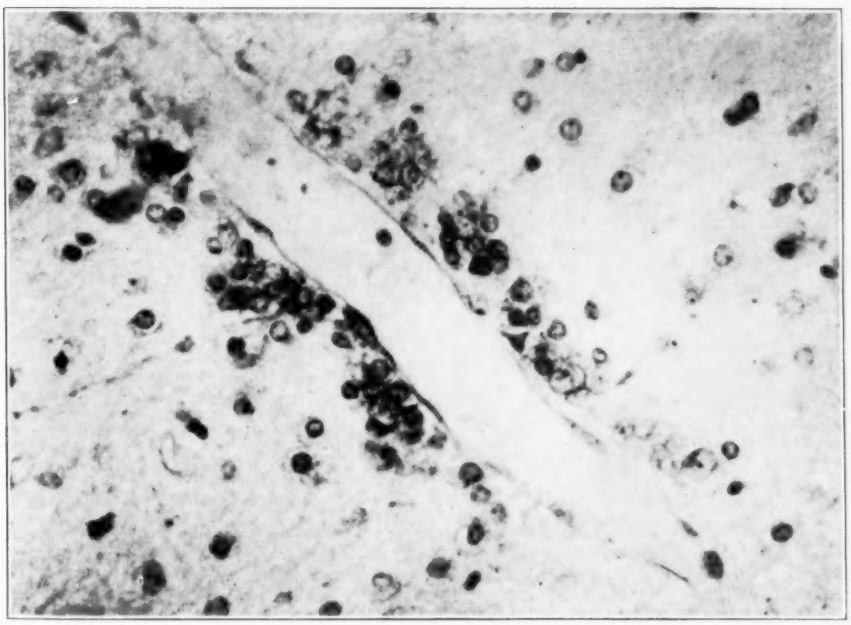


Fig. 4 (case 6).—Photomicrograph showing perivascular glial rim around a small veinous blood vessel from the white matter corresponding to area 18. Toluidine blue stain; reduced from × 440.

The anatomic diagnosis was: chronic ulcerative amebic dysentery, with old perforation of the cecum; amebic abscess of the liver; extensive abdominal adhesions about the cecum; hyperplasia of the mesenteric glands; chronic tuberculosis of the right lung, spleen and bronchial and hepatic lymphatic glands; old pleural adhesions; ascites; bilateral hydrothorax; hydropericardium; slight edema of the scrotum and feet; atrophy of the heart, liver, spleen and kidneys; edema

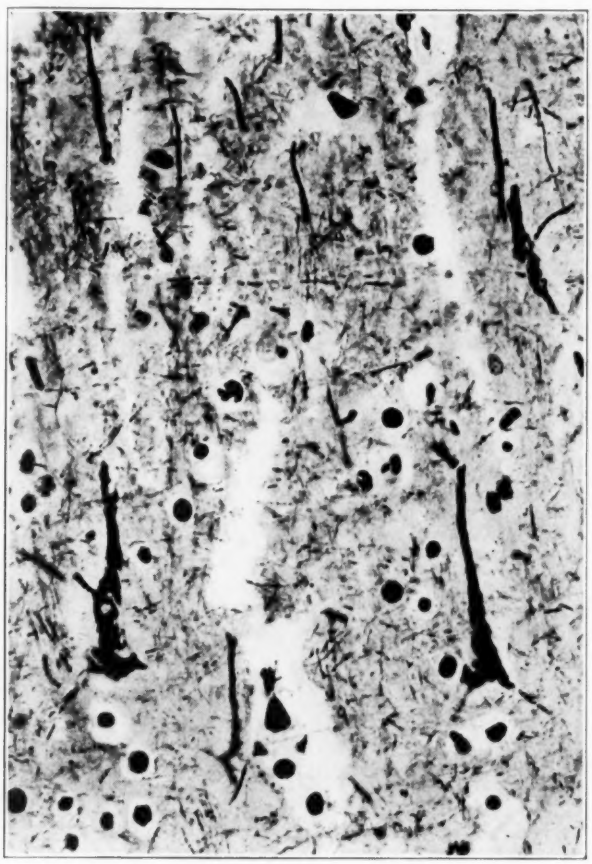


Fig. 5 (case 6).—Photomicrograph showing an area from the frontal cortex (third layer) with marked soaking change: argentophilia, thickening, adhering together, formation of more or less winding strands and breaking or destruction of the intracellular neurofibrils, associated with argentophilia of the nuclei of nervous and glial elements. Silver impregnation of the neurofibrils according to Bielschowsky's method; reduced from × 567.

of the lungs; some atrophy of the frontal convolutions of the brain. The meninges were macroscopically thickened and clouded.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde. Pyroxylin (celloidin) sections were made from the frontal lobe

(area 8), the central region, area 17 with area 18, and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method. Frozen sections were made from the frontal lobe (areas 6 and 8) and were stained according to the methods of Bielschowsky and Herxheimer. Besides these, we made frozen sections stained according to the methods of Bielschowsky, Herxheimer, Spielmeyer, Holzer, Cajal and Globus and Hortega and Globus from the following regions: areas 6, 8, 37 and 17 (with area 18), the central area, the

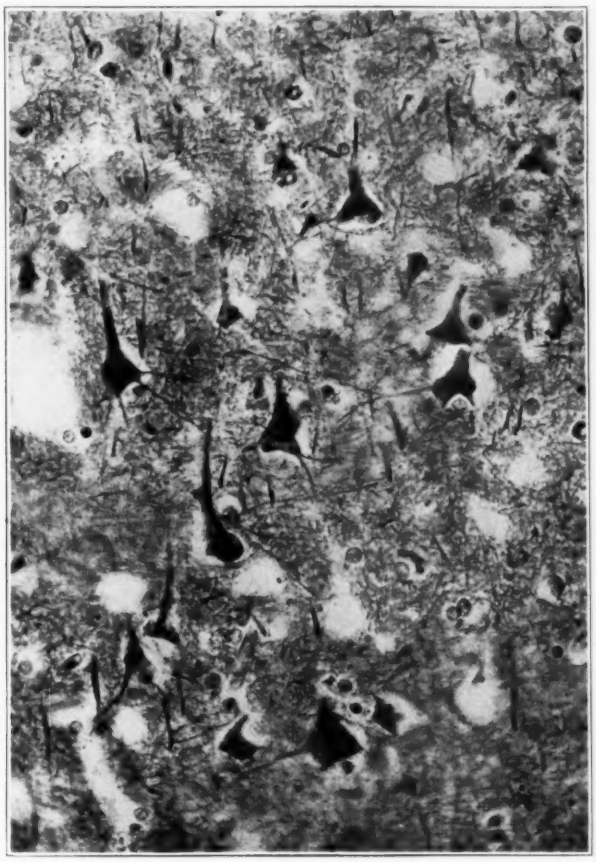


Fig. 6. (case 6).—Photomicrograph showing an area from the frontal cortex (third layer) with normal silver impregnation and no soaking change. The nuclei are light and unimpregnated. Most ganglion cells show entirely normal neurofibrillar structure; only in some instances do the intracellular neurofibrils show a tendency to collect along the margin of the cell or along the nucleus. Figure 7 shows individual cells from this figure with higher magnification. Silver impregnation according to Bielschowsky's method; reduced from × 445.

cornu ammonis and the striatum and pyroxylin sections from areas 6, 10 and 37 and cornu ammonis stained with toluidine blue.

Macroscopic Appearance: Inspection of the brain, fixed in formaldehyde, which was still at our disposal, confirmed the fact, which had already been

observed at autopsy, that the convolutions of the entire frontal lobe were very narrow and the sulci much widened (fig. 1). The convolutions of the temporal, parietal and occipital lobes were about normal in shape; the central convolutions were almost normal, but were slightly narrower than usual. The macroscopic appearance indicated true atrophy but for reasons brought forward by histologic examination we consider the condition as pseudo-atrophy (see also Alexander [23]).

Microscopic Appearance: The meninges were edematous, but not infiltrated or thickened. Throughout the whole cerebral cortex one could observe sporadic small and early deficits of obviously vascular origin in the gray and white matter of the convolutions. Apart from these small ischemic foci (fig. 2), the architecture of the cortex appeared unchanged, if one looked at it with a low magnification. On examination with a higher power magnification,

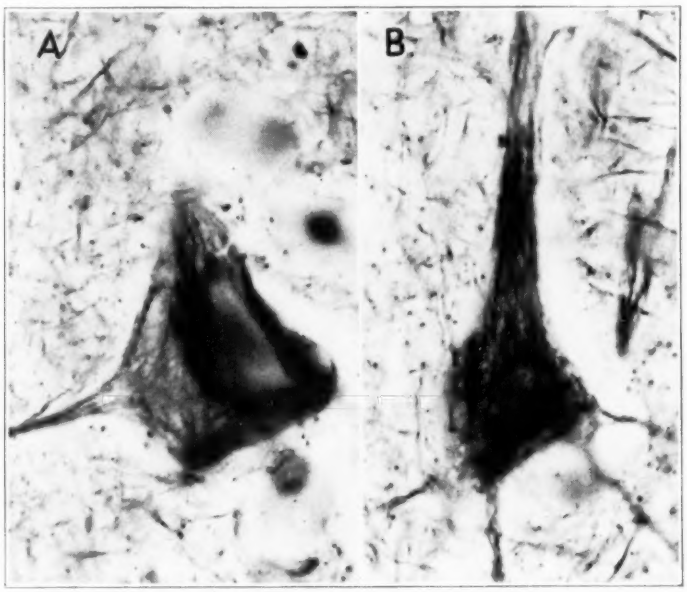


Fig. 7 (case 6).—Photomicrographs of two ganglion cells from figure 6 (third layer of the frontal cortex) with higher magnification. Impregnation is normal: there is no soaking change. *A*, ganglion cell, showing tendency of the intracellular neurofibrils to collect along the nucleus of the cell; the nucleus is light and unimpregnated. *B*, ganglion cell with normal neurofibrillar structure and distribution. Silver impregnation of the neurofibrils according to Bielschowsky's method; oil immersion; × 1,250.

however, one could see that the cortex presented, besides these sporadic pale spots, another slight alteration. A great number of cortical cells appeared not entirely shrunken, but pyknomorphic or even pyknotic (fig. 3 *A*). The pyknomorphic cells were accumulated at certain spots. The glial round and rod cells were increased

23. Alexander, L.: The Neurofibrils in Systemic Disease and in Supravital Experiments, with Remarks on Pseudo-Atrophy of the Brain, Arch. Neurol. & Psychiat. **32**:933 (Nov.) 1934.

throughout the cortex and formed rosettes, which surrounded, clasped and replaced ganglion cells, not only in the deep layers of the cortex but also in the third layer. These rosettes were preferably present around the pyknomorphic cells and were present in the greatest number at the places where the pyknomorphic cells were accumulated. In the white matter the oligodendroglia was increased and formed knots and rims up to four rows of cells along some small veins (fig. 4). There was no increase of macroglia or fibrous glia. The oligodendroglia was also increased in the corpus striatum. Many cortical ganglion cells contained deposits of lipoid, which were also present in cellular elements in the adventitia of some blood vessels; these cells contained also at some places a pigment which stained green or blue-green with toluidine blue and which was probably iron. The pyroxylin sections did not show any postmortem artefacts, with the exception that in specimens stained with toluidine blue, all the cortical ganglion cells, including the nonpyknomorphic examples, appeared somewhat darker stained than usual, thus representing Fortuyn's [24] "noninflated" type. This may be due to the fact that in this case (in contrast to most of the others) the material for the toluidine blue stain was fixed in formaldehyde. However, none of the ganglion cells showed perinuclear retraction spaces.

Specimens stained by the Bielschowsky method showed at some places a marked "soaking change" (Alexander [23]), with argentophilia, thickening, adhering together, formation of more or less winding strands and crumbling or destruction of the intracellular neurofibrils, associated with argentophilia of the nuclei of nerve and glia cells (fig. 5). Even at places that were free from the soaking change (fig. 6) the intracellular neurofibrils showed in some instances the tendency to collect along the margin of the cell and along the nucleus (fig. 7). The newly prepared Bielschowsky specimens showed essentially the same changes as those that were made immediately after fixation; only the degree of the argentophilia was lessened by the long preservation in formaldehyde.

In the cerebellar cortex sporadic glial shrubs were observed which surrounded or replaced some Purkinje cells. Most Purkinje cells, however, were undamaged, showing even good Nissl structure. But the layer of Lannois-Paviot was enlarged and increased throughout the cerebellum, especially at the tops of the gyri and at the corners where they bent to the valleys, reaching there from four to six rows of cells. There was no lobular atrophy.

CASE 7.—*Chronic bacillary dysentery of the mannite-fermenting group; last attack of three and one-half months' duration.*

Clinical History.—A Chinese man, aged 25, a student, had suffered from several attacks of diarrhea during the summers two and three years before admission to the hospital. He was admitted on Oct. 20, 1927, three months after the onset of the last attack, which had started mildly but had become progressively worse until as many as thirty bloody and mucous stools were passed daily.

On admission the patient was extremely emaciated and weak. He had had continuous incontinence during the night before admission. He was dehydrated and exhausted, had lost much weight and appeared pale and weak. Shortly after admission the patient was somewhat irrational and refused to answer questions. The skin was dry and loose; the lips were dry, and the tongue was coated. Beginning decubitus over the coccygeal region was noted on admission. The abdominal reflexes were diminished on the right side.

---

24. Fortuyn, A. B. D.: Histological Experiments with the Brain of Some Rodents, J. Comp. Neurol. **42**:349, 1927.

The diarrhea persisted. On November 1, the patient became increasingly weak and apathetic. The eyeballs rolled upward. On the next day he was drowsy, in spite of therapy (transfusion and injections of dextrose and saline solution). On November 3, the general condition became rapidly worse; the patient became unable to take any food by mouth. He died on November 4, at 6:30 p. m.; respiration stopped ten minutes later than cessation of the heart beat.

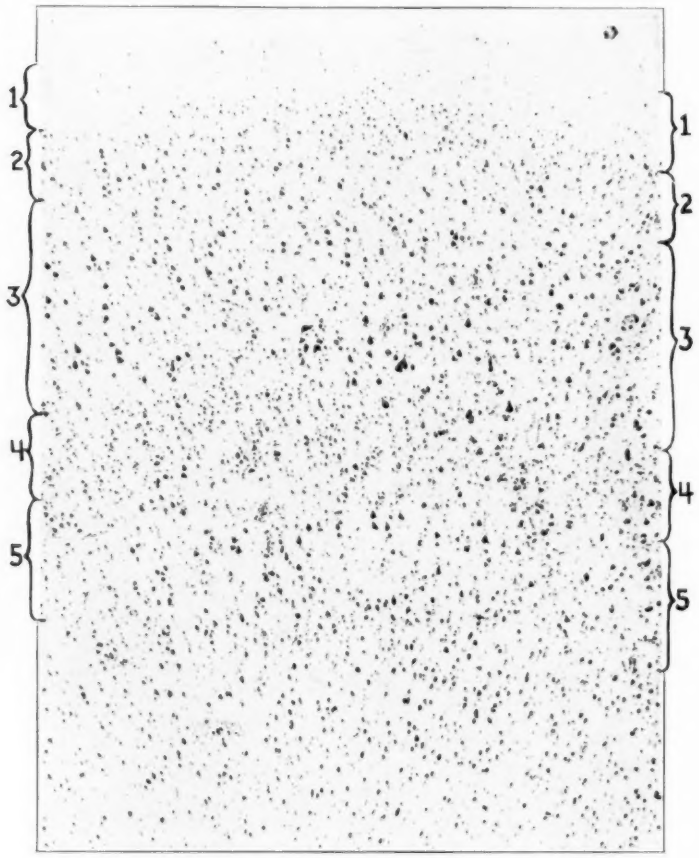


Fig. 8 (case 7).—Photomicrograph of a section from the frontal cortex, showing all layers. In the third and the fifth layer, in about the vertical midline of the figure, small early ischemic foci are visible. The focus in the third layer (slightly to the left of the midline of the figure) with a small venous blood vessel in its center is shown in figure 9 with higher magnification. Toluidine blue stain; reduced from × 64.

Autopsy.—The examination was made twenty-four and one-half hours after death. The body was greatly emaciated, weighing 32 Kg. and measuring 164 cm. in length. There was total atrophy of the subcutaneous fat. The muscles were greatly atrophied. Rigor mortis was present.

The anatomic diagnosis was: bacillary dysentery of the mannite-fermenting group, with chronic ulcerative and subacute diphtheritic colitis; chronic calcified and caseous tuberculosis of the bronchial lymphatic glands; purulent bronchitis, with organizing and more fresh lobular pneumonia; emaciation; anemia; old pleural and peritoneal adhesions; atrophy of the heart, liver and spleen, and hyperplasia of the mesenteric lymphatic glands.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde. Pyroxylin sections were made from the frontal lobe, the central region, area 17 (with area 18) and the cerebellum and were stained with toluidine blue, and hematoxylin-eosin and according to van Gieson's method; frozen sections were made from the frontal cortex and stained according to Bielschowsky's and

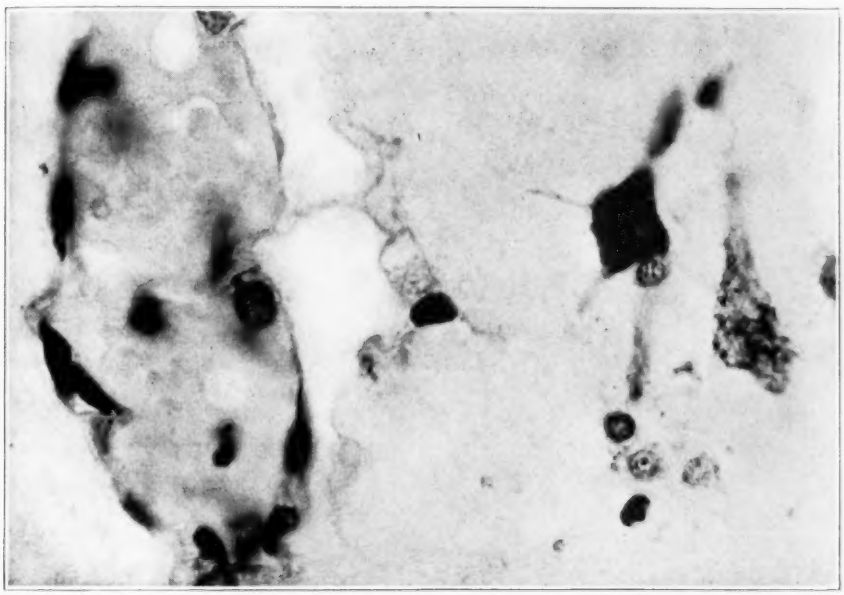


Fig. 9 (case 7).—Photomicrograph showing a detail from the early ischemic focus in the third layer of the frontal cortex from figure 8 with higher magnification. In the immediate neighborhood of the small venous blood vessel in the left half of the figure a monster glia cell is seen, occupying the middle of the figure. In the right half of the figure are three severely altered ganglion cells; that in the left upper part showing pyknosis, that on the right side of this showing shadow cell formation and the third, in the lower part of the picture, under the pyknotic cell, showing acute colliquefaction, with expulsion of the nucleus and karyorrhexis, the cell body being replaced by three glia cells. Only the apical dendrite, melted off from the destroyed cell body, is still visible. Toluidine blue stain; oil immersion; reduced from × 1,290.

Herxheimer's methods. Besides these sections, which were made soon after autopsy, we stained additional specimens from areas 6 and 10, the central area, area 17 (with area 18), area 37, the cornu ammonis, the caudate nucleus, the optic thalamus and the lenticular body, according to the methods of

Bielschowsky, Herxheimer, Spielmeyer, Cajal and Globus and Hortega and Globus, Penfield and Holzer. Additional pyroxylin sections were made from areas 6, 10 and 37, the cornu ammonis and the brain stem and were stained with toluidine blue.

Macroscopic Appearance: The frontal lobe was slightly pseudo-atrophic; the convolutions were narrow, and the sulci wide. But the pseudo-atrophy was less marked in this case than in case 6; therefore, it was not mentioned in the original record of the autopsy.

Microscopic Appearance: The meninges were slightly edematous at some places, but in all other respects were normal. Sporadic early small ischemic foci were present all over the gray matter of the cortex (figs. 8, 9 and 10). In the

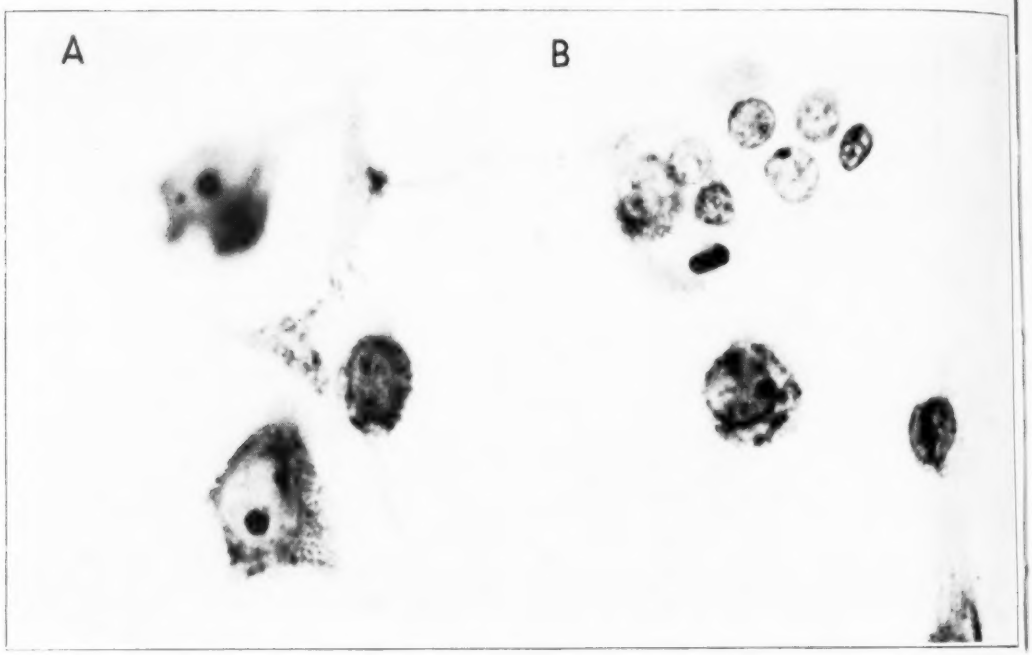


Fig. 10 (case 7).—*A*, photomicrograph showing an ischemic cell from the margin of a small early ischemic focus in the third layer of the frontal cortex. The nucleus of this cell is characteristically dark, and the protoplasm is pale; the apical dendrite is melting off. The two cells to the left are normal. *B*, photomicrograph showing a glial star replacing a ganglion cell, from the margin of a small early ischemic focus in the third layer of the frontal cortex. Both *A* and *B* were taken from the edges of the same ischemic focus in the third layer, a little to the left of the midline of figure 8, from which figure 9 was also taken. Toluidine blue stain; oil immersion, × 1,290.

white matter and the brain stem only here and there was some rare, small perivascular disintegration. Apart from the small sporadic ischemic foci, the architecture of the cortex, if one looked at it with a low power magnification, appeared grossly unchanged (fig. 8). On examination with higher magnification one could observe outside the ischemic foci among the normal cells, especially in

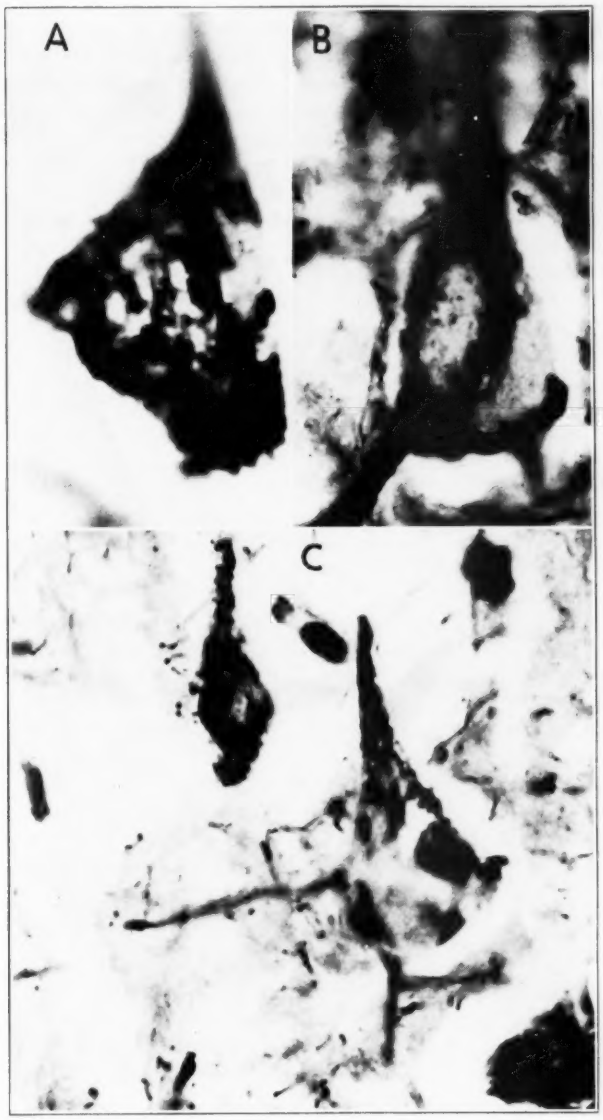


Fig. 11 (case 7).—Photomicrographs showing ganglion cells from the third layer of the frontal cortex presenting soaking change. *A*, argentophilia, thickening, adhering together; *B*, formation of thick, winding argentophilic strands; *C*, argentophilia, thickening, breaking, crumbling and destruction of the intracellular neurofibrils, associated with argentophilia of the nuclei of nervous and glial elements. The argentophilic, impregnated nucleus of the larger cell in *C* should be noted especially. Silver impregnation of the neurofibrils according to Bielschowsky's method; oil immersion; magnification, *A*, × 1,940; *B* and *C*, × 1,290.

the third layer and in the layers basal to it, a number of pyknomorphic cells, more or less surrounded by glial rosettes. These cells were not as numerous in this case as in case 6; corresponding to this fact, this case showed also not as many glial stars (ganglion cell replacements) in these layers, but they were present here in all the layers. Some rather rare cells throughout the cortex contained moderate amounts of lipoid: lipoid was also present in the adventitia of some blood vessels. Only in the cornu ammonis was the content of lipoid in the ganglion cells more rich than anywhere else in the cortex: Here all large cells of the dense, as well as of the loose, ribbon contained considerable amounts of lipoid. A number of small blood vessels in the white matter showed perivascular nodules or rims of oligodendroglia cells. In rare instances one could see a perivascular glial node, which showed also production of glial fibers and which was recognizable in Holzer specimens. The blood vessels themselves were essentially unaltered. All the pyroxylin sections, especially those stained by the Nissl method, took the stain successfully and did not show any postmortem changes. Sporadically, especially along the edges of the blocks but also in other large and small areas inside, the Bielschowsky specimens showed a marked typical soaking change of the neurofibrils, with argentophilia, thickening, formation of more or less winding strands and breaking or crumbling of the intracellular neurofibrils, associated with argentophilia of nuclei of the nerve and glia cells (fig. 11). This case is of interest because along with large areas of argentophilia there were also very small ones, represented by only two or three nerve cells, which showed the same change; at these places the nuclei of the immediately surrounding glia cells were also argentophilic, however, thus indicating the nature of the neurofibrillar alteration. All other cells outside the argentophilic areas showed normal impregnation of neurofibrils with the Bielschowsky method of staining, with unstained nuclei of ganglion and glia cells. In contrast to case 6, the argentophilic areas of the newly prepared Bielschowsky specimens, which were made five and one-half years after fixation, showed the same high degree of argentophilia as the old ones; they were present in only two blocks, however—one of area 10 and one of area 6 of the frontal lobe.

The cerebellar cortex showed increase of Lannois-Paviot's layer, especially at the tops of the gyri and at the corners of these tops; only in rare places was there fresh, beginning, progressive shrub formation along the dendrites of some damaged Purkinje cells.

CASE 8.—*Bacillary dysentery of the Shiga type, of about five weeks' duration.*

Clinical History.—A Chinese man, aged 25, a soldier, had experienced the sudden onset of the disease about one month before admission, with chilliness, feverishness and obstinate constipation. Severe general symptoms were described by the patient: mental cloudiness, headache and general malaise. The patient said that he was unconscious from the third day of the disease for about one week. Three weeks before admission severe diarrhea, with blood and mucus, developed.

On admission (Sept. 14, 1928) the patient appeared "dull and stupid" and of a "neurotic disposition." He was weak and undernourished. The knee jerks and ankle jerks were not obtained, while the biceps, triceps and radial reflexes were present. On September 21, the patient appeared miserable. He had frequent stools, with little blood and mucus, however. On September 21, at 3 p. m., after having used the bed pan, he suddenly had convulsions of tonic type, with marked opisthotonos, the neck being rigid and arched backward and the mouth being wide open. The patient died almost instantly in this convulsive attack.

Autopsy.—This examination was made seven and three-quarter hours after death. The body weighed 41 Kg. and measured 171 cm. The skin was dry and wrinkled. There was no edema. There were slight atrophy of the subcutaneous fat and undernutrition of the abdominal muscles, which were pale and flabby.

The anatomic diagnosis was acute ulcerative colitis (Bacillus dysenteriae Shiga), acute splenic tumor, fibrous pleural and peritoneal adhesions and ascariasis.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde. Pyroxylin sections were made from the frontal lobe (area 8), area 17 (with area 18), the central region and the cerebellum and were stained

Fig. 12 (case 8).—Photomicrograph showing focus of perivascular ischemic disintegration in the convolutional white matter of area 18. Stain of the myelin sheaths according to Spielmeyer's method; × 155.

with toluidine blue, hematoxylin-eosin and by van Gieson's method. Besides these sections, found in the collection, we made frozen sections from areas 10, 6, 37 and 17 (with area 18), the central area, the cornu ammonis, the caudate nucleus, the lenticular body, the optic thalamus and the cerebellum, stained according to the Bielschowsky, Herxheimer, Spielmeyer, Cajal-Globus, Hortega-Globus and Holzer methods.

Macroscopic Appearance: The convolutions of the frontal lobe were slightly narrower and the gyri somewhat wider than usual, but the condition was not gross enough to be definitely called pseudo-atrophic, at least not without the data of measurement of the differential between capacity of the skull and the volume of the brain, which, unfortunately, were not at our disposal.

Microscopic Appearance: The meninges were unaltered. Sporadic ischemic foci were present in the gray matter of the cortex. Only a few of the cells within these foci, such as were still left and had not entirely disappeared or been replaced by small glial rosettes, showed the characteristic ischemic change. Most of them were merely pale and showed cell shadows, some of them more or less clasped by glia cells. Outside the foci also some single ischemic or "shadow" cells were seen among normal cells, but no pyknomorphic cells were present. Glial reaction in the form of rosettes surrounding or replacing ganglion cells was observed almost solely within the ischemic foci and only in rare instances outside them. Some cells showed perinuclear retraction spaces (postmortem change), but the number of these cells was small and the degree of the change slight; no other artefacts were present in the Nissl picture. In the white matter some rare perivascular glial rims were visible. Some foci or perivascular ischemic disintegration were present in the white matter of the cortex (fig. 12); none was seen in the brain stem.

The Bielschowsky specimens showed at various places the characteristic soaking change. The cerebellum showed in sporadic places an increase of Lannois-Paviot's layer to from five to seven rows of cells, and, in rare instances, small regressive shrub formation, with dark-stained glia cells that were poor in processes.

CASE 9.—*Chronic bacillary dysentery of the mannite-fermenting group; last attack of about five weeks' duration.*

Clinical History.—A Chinese man, aged 49, a laborer, had suffered three years before admission from a short attack of dysentery. More than one month before admission there was the onset of an acute severe attack, with watery and bloody diarrhea. There was marked general weakness. For twenty days the patient had had no appetite for food and had confined himself to water. For ten days he had had insomnia and deafness.

On admission, on Oct. 17, 1927, the patient appeared markedly dehydrated, emaciated, exhausted and weak. The skin was dry, loose and dusky brownish, with leukodermic patches. The lips were dry and cracked; the tongue was coated. The eyeballs were sunken, and there was epiphora. In both eyes there were xerophthalmia with Bitot's spots and early ulcers of the cornea, apparently keratomalacia. Hearing was slightly impaired on both sides. The facial expression was dull. The tendon reflexes were not easily elicited. The pulse rate was 100 a minute, but regular.

Within the next few days peritonitis developed. On October 19 and 20, there was profuse sweating. On October 21, the condition became progressively worse. The patient became drowsy. He died at 5:05 p. m. Respiration and the heart beat ceased at about the same time.

Autopsy (one week after death).—The anatomic diagnosis was: chronic bacillary dysentery, with extensive ulceration and perforation of the wall of the colon; acute generalized fibrinopurulent peritonitis; scattered caseous tubercles in the apexes of the lungs; early bronchopneumonia; old fibrous pleural adhesion (left); early arteriosclerosis; leukoderma; corneal ulcer; emaciation; marked postmortem change; old calcified tuberculosis of the lung; focal necrosis in the liver, and atrophy of the spleen and pancreas. The brain was macroscopically unaltered.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal lobe, the central region and the cerebellum and were

stained with toluidine blue and hematoxylin-eosin and by van Gieson's method; frozen sections were made from the frontal lobe and stained according to the Bielschowsky method.

Microscopic Appearance: The meninges were edematous at some places but in other respects normal. The architecture of the cerebral cortex appeared under a low magnification to be almost normal; in only a few places were small perivascular foci of disintegration seen; so far as they were still present the nerve cells in these places appeared as shadow cells (fig. 13), but some also showed the characteristic ischemic change. Yet ischemic foci were rare in this brain, in contrast with those previously described. The chief feature in this brain was the considerable productive activity of the glia outside the ischemic foci. It formed a large number of rosettes and stars, which clasped and replaced ganglion cells

Fig. 13 (case 9).—Photomicrograph showing ganglion shadow cell, from a small early ischemic focus in the third layer of the frontal cortex. Toluidine blue stain; oil immersion; × 2,500.

(fig. 14), not only in the deep layers but also in the third layer; the second and first layers were practically free. The clasped ganglion cells were mostly pyknomorphic or even pyknotic. Some showed also the characteristic ischemic change. The clasping glia cells were oligodendroglia cells or rod cells, as in the other cases. Besides these glial stars, the cortex presented another pathologic feature—the presence of a number of ischemic cells and shadow cells, without surrounding glial reaction, scattered throughout the cortex. Besides all these definitely pathologic forms of cells, a considerable number of sporadic cells were present, which showed postmortem changes, with extensive perinuclear retraction spaces around a normally but somewhat smaller and darker nucleus and a not sharp outer border to the protoplasm.

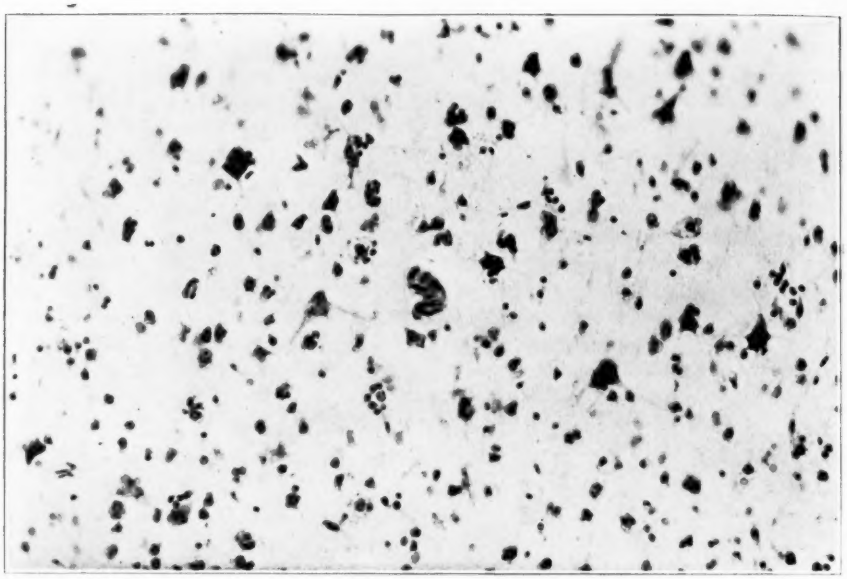


Fig. 14 (case 9).—Photomicrograph of a section from the third layer of the frontal cortex, showing the productive activity of the glia outside the ischemic foci. Numerous glial rosettes and stars clasp pyknomorphic and pyknotic ganglion cells and replace them. Besides these, some small glial nodules along capillaries are also visible. Toluidine blue stain; reduced from × 300.

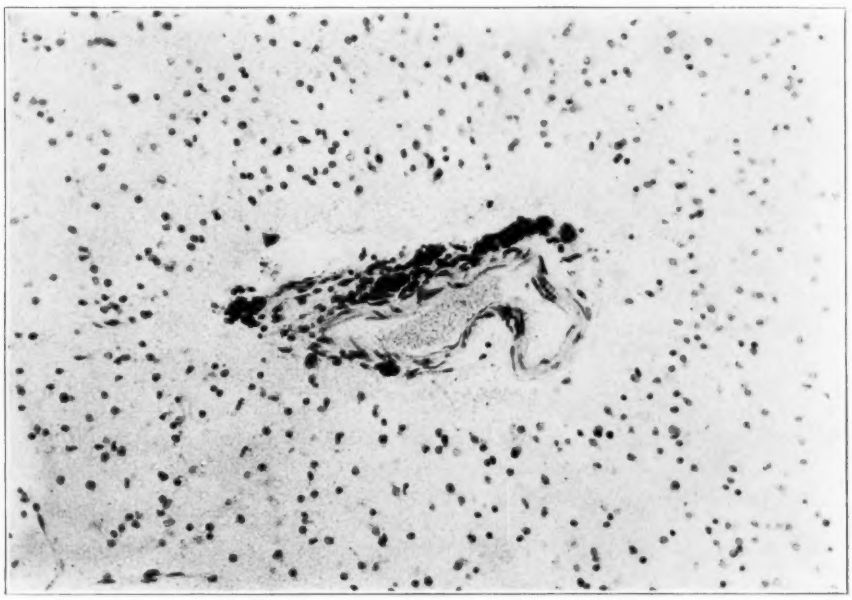


Fig. 15 (case 9).—Photomicrograph showing a blood vessel in the white matter of the frontal lobe. Products of breakdown stained green with toluidine blue are collected in large phagocytic cells in the adventitia. Toluidine blue stain; reduced from × 300.

There were no continuous perivascular glial fences, but glial knots were present along some small vessels and capillaries. There was a slight increase of the perivascular glial rims surrounding the larger blood vessels. Products of breakdown, stained green with toluidine blue, were collected in large cells in the adventitia of some larger blood vessels (fig. 15). In rare single spots (twice in our specimens) there was lymphocytic infiltration of veins at the corticomyelin border.

The Bielschowsky specimens showed the characteristic soaking change, with argentophilia of all nuclei and argentophilia, thickening, breaking and, in most instances, practical disappearance of the intracellular neurofibrils, but only at the outer part of the block, while the interior parts appeared somewhat pale, brownish, uniform, but essentially normal.

The cerebellar cortex showed thickening and increase of Lannois-Paviot's layer in some places, especially at some corners of the tops of gyri. Only one glial shrub was seen in these specimens.

CASE 10.—*Amebic dysentery (last attack of twenty-five days' duration) complicated by seropositive syphilis and miscarriage at six months of pregnancy; spontaneous abortion in the hospital on the day of admission.*

Clinical History.—A Chinese woman, aged 29, a housewife, had had previous attacks of dysentery every summer for the preceding two years. The beginning of the last attack was twenty days before admission, with frequent mucous and bloody stools.

On admission (Sept. 30, 1927), the patient appeared very ill, emaciated, weak and pale, but was fairly well nourished and not dehydrated; she was mentally alert. The pulse was rapid and weak, but regular. The general condition and circulation became worse after the beginning of treatment with emetine and bismuth subnitrate. Four days after admission death occurred in circulatory collapse.

Autopsy (twelve hours after death).—The anatomic diagnosis was: acute ulcerative colitis (amebic dysentery), with perforation of the wall of the descending colon, followed by localized fibrinous purulent peritonitis; acute splenic tumor; congestion of the lungs; slight pleural effusion; multiple congenital cysts of the kidneys and liver; postpartum uterus, with acute endometritis; corpus luteum and follicle cysts in the left ovary; fatty change of the kidneys, and hypertrophy of the "chief cells" of the hypophysis. The brain macroscopically was unaltered.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal lobe, the central region, area 17 (with area 18) and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal. In the cerebral cortex there were sporadic small ischemic foci. Outside the foci, in the third to the sixth layers, but accentuated only in certain places, there was considerable progressive activity of the glia, consisting in surrounding and replacing of ganglion cells, which, so far as they were still present, showed pyknomorphism. In the white substance in only a few places in the sections from the frontal and occipital lobe did the small blood vessels show perivascular glial fences or knots. In the cerebellum an increase of Lannois-Paviot's layer to from four to six rows of cells was present at places; there was no shrub formation.

CASE 11.—*Bacillary dysentery of the mannite-fermenting group (attack of twenty days' duration), complicated by arteriosclerosis, chronic nephritis and emphysema of the lungs.*

Clinical History.—An American man, aged 66, a clergyman and teacher, had suffered from dysentery thirty-four years before admission. After the onset of the last illness, with diarrhea, nausea, vomiting and fever, he had cramps in the legs and the back. On the next day he was delirious, after having taken some opium tablets.

On admission (July 31, 1929), four days after the onset, the patient was weak and prostrated, but the mental state was clear. The next week there were increasing dehydration, weakness and apathy. On August 12, he was drowsy; on August 14, he was semiconscious. Death occurred on August 15, after twenty days' duration of the disease.

Autopsy (twenty-six and one-half hours after death).—The anatomic diagnosis was: acute ulcerative enterocolitis (B. dysenteriae), with perforation; early acute fibrinous peritonitis; degeneration of the myocardium, suprarenal glands and liver; acute splenic tumor; emphysema of the lungs; hydrothorax; pulmonary edema; diphtheritic bronchitis and tracheitis; localized necrosis of the lung; dehydration; malnutrition; generalized arteriosclerosis; chronic nephritis; hypertrophy of the prostate; slight hydro-ureter; hyaline and fibrous tuberculosis of the lungs, with chronic tuberculous pleurisy; adenoma of the kidney; slight convolutional atrophy of the brain. The meninges were cloudy and thickened. Dilatation of lateral and third ventricles was present.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal lobe, the central region, area 17 (with area 18), the optic thalamus and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: There was proliferation of the intima and adventitia of some cortical vessels. Sporadic ischemic foci were present; one larger one in the form of a vertical strip cut through all the layers of the cortex. All the other foci in these specimens were small. There was generalized productive increase of glial round and rod cells throughout the cortex, from layer 2 to layer 6, with many claspings and replacements of ganglion cells. Fences and knots of oligodendroglia were present around the small blood vessels in the white substance. Postmortem changes (holes) were present in the white substance and in the internal capsule. In the cerebellum there were dilatated blood vessels, but no other changes.

Case 12.—*Bacillary dysentery of the mannite-fermenting group, the last attack of eighty days' duration.*

Clinical History.—A Chinese, aged 42, a rickshaw man, gave a history of frequent diarrhea (from one to four times a year) during the past twenty years. He had had a severe attack of dysentery for two months.

On admission, on Nov. 24, 1926, the patient was extremely emaciated and had lost much weight. There was severe dehydration, with a dry scaly skin and a scaphoid abdomen. There was marked general weakness, with some psychic impairment. The patient appeared to be too weak to cooperate much; he lay listlessly in bed, without interest in his surroundings. The pupils were regular and equal, but reacted sluggishly to light and in accommodation. There were secondary anemia, necrotizing stomatitis and atrophy of the tongue.

The diarrhea persisted. On December 4, the patient had become too weak to stand, and on December 11, to speak aloud. The condition became progressively worse. On December 13, the pulse rate was 124 beats a minute. On December 14, at 7 p. m. the patient collapsed. The pulse became rapid and weak; respiration

was irregular, and the hands and jaws showed trembling. At 9 p. m. he died; the pulse and respiration ceased at the same time.

Autopsy (thirty hours after death).—The body measured 116 cm. in length and weighed 32 Kg. It showed extreme emaciation, the subcutaneous fat being very thin and atrophic. The muscles were thin and anemic.

The anatomic diagnosis was: bacillary dysentery, with subacute ulcerative colitis and thickening of the wall of the colon; hyperplasia of mesenteric and retroperitoneal lymphatic glands; hyaline and caseous pulmonary tuberculosis, with early cavity formation; thickening and calcification of the pleura; lobular pneumonia; acute fibrinous pleurisy, with effusion; hypoplasia and gelatinous degeneration of the bone marrow. The meninges were edematous and slightly turbid.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal cortex, the motor region, area 17 (with area 18), the cerebellum and the thoracic and lumbar segments of the spinal cord and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were edematous. Small ischemic foci were present in the gray matter of the cortex; there was no other gross disturbance of the architecture. Apart from these changes, individual ischemic and pyknomorphic cells were scattered throughout the cortex. Glial rosettes, which clasped and replaced the damaged ganglion cells, were present in the third to the sixth layer of the cortex. Products of breakdown, stained green with toluidine blue, were present in the adventitia of some middle-sized blood vessels in the white matter. In the cerebellar cortex there was typical homogeneous change of some Purkinje cells, with the formation of extensive large shrubs sporadically in places. The spinal cord was without pathologic changes.

CASE 13.—*Bacillary dysentery of the mannite-fermenting group, of five months' duration, complicated by pulmonary and intestinal tuberculosis.*

Clinical History.—A Chinese, aged 34, a rickshaw man, at the beginning of the disease had also headache and dizziness. During the course of the disease secondary anemia developed. There were severe emaciation, dehydration and dry skin, with slight desquamation, especially on the legs. There were fever, nausea, vertigo and headache. After increasing exhaustion and loss of strength, the patient died on April 4, 1927, at 8 a. m.

Autopsy (on the day of death, probably from two to seven hours after death).—The body was greatly emaciated, measuring 170 cm. and weighed 36 Kg.

The anatomic diagnosis was: chronic caseous pulmonary tuberculosis, with cavity formation and perforation of the pleura of the left lung; pyopneumothorax on the left; caseous lobular pneumonia; old fibrous pleural adhesions on the right; caseous tuberculosis of tracheobronchial and mesenteric lymph nodes; chronic ulcerative colitis; extensive tuberculosis of the colon; tubercles in the liver; scarring of the kidneys; atrophy of the pancreas; hyperplasia of the bone marrow; fatty liver; early arteriosclerosis. The meninges were thick, the ventricles were slightly dilated.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal cortex, the central region, area 17 (with area 18), the brain stem (the caudate nucleus with the internal capsule and lenticular body) and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: There was fibrosis of the meninges, with an increase of cells in places, but no definite infiltration. There were only rare and small ischemic foci. The cortical architecture in other respects was grossly unaltered. Throughout the cortex in layers 3 to 6 there was progressive increase of round and elongated glial elements, with clasping of pyknomorphic ganglion cells and shadow cells, which one could see sporadically scattered, as well as glial replacement of ganglion cells. In sporadic places in the white matter and, more rarely, in the gray matter, there were oligodendroglial rims surrounding small blood vessels. In the cerebellar cortex there was an increase of Lannois-Paviot's layer to from four to six rows in sporadic places, especially at the corners of the tops of some gyri, but no glial shrubs. In the brain stem there was an increase of the subependymal glia; no other changes were seen there.

CASE 14.—*Bacillary dysentery of the Shiga type (last attack of five weeks' duration) and amebiasis, complicated by syphilitic cirrhosis of the liver.*

Clinical History.—A Chinese man, aged 49, a miller, with a history of syphilis, about two years before admission had had transitory shooting pains and an unsteady gait. Severe and long attacks of dysentery had occurred six years and twenty months before. For three weeks he again had had acute dysentery and bloody diarrhea.

On admission, on Aug. 24, 1926, the patient was emaciated and weak; the eyes were jaundiced, and there were ascites and edema of the legs up to the knees. The knee and ankle jerks were not obtained.

On August 29, the patient grew weaker and appeared very ill. Gradually a psychotic condition developed: He was very miserable at times and complained of homesickness. He asked and struggled for discharge; on the next day he became noisy, unreasonable and mentally sluggish, but not disoriented. He was discharged against advice on August 30. Six days later he returned to the hospital. Diarrhea had persisted. The patient was much emaciated and dehydrated. The temperature was subnormal and the pulse feeble and rapid. The skin showed jaundice and areas of subcutaneous hemorrhage. Mentally the patient was irrational; he refused to answer questions or to be disturbed. The reflexes were absent. On September 6, at 8 p. m., he had a profuse gush of blood from the mouth. After that he was drowsy; the pulse was weak, and he later became comatose. On September 7, at 1 p. m., Cheyne-Stokes breathing appeared, and the pulse could no longer be felt. Death occurred at 2:30 p. m.

Autopsy (about nineteen and one-half hours after death).—The anatomic diagnosis was: syphilitic cirrhosis of the liver, with multiple gummas; splenomegaly; ascites; gummas in both testes; scarring of the pancreas; adhesions around the liver and spleen; ulcerative colitis; confluent lobular pneumonia, and edema in the lower lobes of both lungs; a scar on the prepuce; hemorrhage in the skin over the chest; parenchymatous degeneration of the kidneys, with fatty changes and calcification; fatty heart. The brain macroscopically was unchanged.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal cortex, the central region, area 17 (with area 18), the lentiform nucleus and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal. In the cerebral cortex there were small ischemic foci. Outside these foci were numerous glial rosettes, surrounding and clasping pyknomorphic and even pyknotic ganglion cells, which were scattered in considerable numbers through the cortex. Replacement of

ganglion cells had occurred in layers 3 to 6. Products of breakdown, stained green with toluidine blue, were present in a number of perivascular phagocytic cells around small and middle-sized blood vessels in the white matter of the cortical convolutions. In the cerebellar cortex there was at places an increase of Lannois-Paviot's layer to from four to six rows of cells; only in rare instances was there also surrounding of damaged Purkinje cells and the beginning of their dendrites by glia cells; there was no definite shrub formation. In the brain stem no essential pathologic changes were determined.

CASE 15.—*Amebic dysentery, complicated by atrophic cirrhosis of the liver and ankylostomiasis.*

Clinical History.—A Chinese man, aged 37, a farmer, had suffered from dysentery ten years before admission. Distention of the abdomen and swelling of the legs and scrotum had been present for three months. Bloody diarrhea had existed for thirteen days.

On admission, on Sept. 3, 1925, there were emaciation, pallor, icterus, tachycardia, fever, ascites, collateral portal circulation, secondary anemia and edema of the legs and external genitalia. The patient's mind was clear, but marked weakness and decrease of spontaneous activity were observed. He was moderately uncomfortable and extremely apprehensive. The knee jerks were absent.

Emaciation, weakness and anorexia gradually increased. In spite of the fact that fluid had accumulated in the abdomen, the body and extremities were dried up and greatly emaciated. There was marked dehydration of the body tissue. On October 25, the patient became incontinent and later unconscious. On October 26, at 12:35 a. m., the pulse became inpalpable. Death occurred at 1 a. m.; the heart beat ceased before respiration.

Autopsy.—(Formaldehyde was injected into the body eleven hours after death, and the brain was removed thirty hours after death). The anatomic diagnosis was: nodular cirrhosis of the liver; splenomegaly; ascites; wounds from paracentesis; fibrinous peritonitis (cocci in chains found in sections); hemorrhages in the peritoneum; healing colitis, with thickening of the wall of the colon; chronic perisplenitis; uncinariasis; hyperplasia of mesenteric and retroperitoneal lymph nodes, and hyperplasia of the bone marrow of the femur. The brain was without macroscopic changes.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal and parietal lobe, the central region, areas 17 and 18, the cerebellum and the medulla oblongata.

Microscopic Observations: The meninges were unaltered. A great number of the small blood vessels of the cerebral cortex showed thickening and hyalinization of the media. A number of small ischemic foci were present in the gray matter of the cortex. There was general progressive change of the glia, with clasping of pyknomorphic ganglion cells and replacement of a considerable number of ganglion cells scattered throughout the cortex in layers 3 to 6. Perivascular phagocytic cells were present around some blood vessels in the gray and white matter, containing products of breakdown which stained green with toluidine blue. In the cerebellar cortex there were sporadic but large glial shrubs.

CASE 16.—*Bacillary dysentery of the mannite-fermenting group, of three months' duration, complicated by seropositive syphilis.*

Clinical History.—A Chinese, aged 40, a rickshaw man, had had diarrhea with blood and mucus for three months. Swelling of the legs and eyelids had been present for about a week. There were loss of weight and energy, general malaise and anorexia.

On admission (Sept. 12, 1930), the patient appeared markedly undernourished and emaciated, lying in bed with a dull expression of illness. There were ascites and pitting edema of the legs and feet, slight edema of the wall of the chest and edema of the face and eyelids. The edema was nutritional in nature. There was marked dehydration of other parts of the body; the skin was dry and dark. Two bed sores were present over the right side of the back. The lips were dry and pale. The pulse was weak and feeble. Respiration was labored. There were secondary anemia and keratomalacia in both eyes. The knee jerks were sluggish. The mental state was unclear and dull; the patient was unable to talk well. On the following day the general weakness had increased. On September 14, the heart action became feeble, and the patient collapsed and died at 8 p. m. The heart ceased to beat before respiration stopped.

Autopsy (thirty-eight and one-half hours after death).—The body was greatly emaciated. The anatomic diagnosis was: chronic ulcerative colitis and proctitis (B. dysenteriae), with abscess in the submucosa of the lower part of the rectum; internal hemorrhoids; fresh, infected and old thrombi in the hemorrhoidal and prostatic plexus, with extension into the left internal and external iliac veins; pulmonary thrombosis, with septic infarction and abscess of the lung; acute bilateral hemorrhagic fibrinous pleuritis, with effusion; thrombosis of the intercostal and azygos veins; bacterial endocarditis of the mitral valve, with fresh vegetations; thrombosis of the renal arteries; infarcts of the kidney; a small infarct of the pituitary gland (anterior lobe); ascites; edema of the legs; endocardial thickening in the left ventricle; syphilitic aortitis and arteriosclerosis of the aorta, with calcification, ulceration and thrombosis; chronic caseous tuberculosis of the right apex; fibrous pericarditis and pleuritis; fatty change in the liver; marked edema and cloudy swelling of the kidneys; marked emaciation and atrophy of the liver, pancreas and muscles; hyaline change of the splenic arteries; slight emphysema of the lungs; corneal ulcers. The brain and meninges macroscopically were normal.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the central region, areas 17 and 18, the cerebellum and the medulla oblongata, stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal in most of the places examined; only one blood vessel, in the depth of a sulcus over area 18, showed lymphocytic infiltration. Areas 17 and 18 were histologically almost unaltered. In the central region, however, one large early ischemic focus and a number of small early ischemic foci were present. In addition to these foci, the glia was here progressively changed and clasped a number of pyknomorphic and ischemic cells, and replacements of ganglion cells were frequent in layers 3 to 6. Some blood vessels in the white matter contained products of breakdown in perivascular cells, which stained green with toluidine blue. In the cerebellar cortex there was an increase of Lannois-Paviot's layer to from four to six rows of cells in some places; rarely there were also glial shrubs, where Purkinje cells were destroyed or severely damaged. The medulla oblongata was essentially unaltered.

CASE 17.—*Bacillary dysentery (Shiga type) of five days' duration.*

Clinical History.—A Chinese girl, aged 5, was admitted on July 29, 1927, four days after the onset of the illness.

On admission, the child's mind appeared clear. On the evening of the same day she became more toxic and somewhat irrational and restless. The next morning, at 3 a. m., psychomotor excitement had developed; the child was restless,

throwing herself about constantly and talking "a great deal of nonsense." The pulse was almost imperceptible; the heart action was rapid and weak. Death occurred nine hours later, on July 30, at 11:50 a. m.

Autopsy (four hours and forty minutes after death).—The body was well developed and well nourished. The anatomic diagnosis was: bacillary dysentery, with acute diphtheritic ileocolitis; hyperplasia of the mesenteric lymph glands; fatty liver; acute splenic tumor; cloudy swelling of the liver and kidneys; hyperemia of the brain and meninges, and thickening of the meninges.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal cortex, the central region, area 17 (with area 18) and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges at some places were thickened and rich in fibroblasts; at other places, especially over the frontal lobe and cerebellum, were small spots of mononuclear infiltration. In the cortex a number of small characteristic early ischemic foci were seen. Of the few ganglion cells left in these foci, some showed the characteristic ischemic change with dark nuclei and homogeneous, pale shrunken protoplasm; others formed shadow cells. Some glial stars were also present in these foci. In the cerebellar cortex there was an increase of Lannois-Paviot's layer at some sporadic places, but no shrub formation.

CASE 18.—*Bacillary dysentery of the mannite-fermenting group, of more than four months' duration.*

Clinical History.—A Chinese boy, aged 3, who had had a previous attack of dysentery at 2 years of age, had a mucous and bloody diarrhea, of four months' duration.

On admission (Oct. 12, 1929), the child was extremely emaciated and dehydrated. The skin was dry, loose and inelastic. There was atrophy of subcutaneous fat. Xerosis and keratomalacia in both eyes had developed five days before admission. Slight edema (nutritional) was present over the lower part of both legs and both feet. The knee jerk was present on the right, but absent on the left. The eyeballs were deeply sunken. Respiration was slow and irregular. The child was uncooperative, but his mind was clear. Lumbar puncture, on October 13, showed a positive Pandy reaction, with a normal cell count (1 per cubic millimeter).

During the further course the child appeared irritable. On October 18, there was slight rigidty of the neck. On the next day the pulse became feeble, and respiration was shallow and slow. Death occurred on October 19, at 7:30 p. m.

Autopsy (thirty-nine and one-half hours after death).—The anatomic diagnosis was: chronic ulcerative colitis (B. dysenteriae); keratomalacia (bilateral), with perforation of right cornea; confluent lobular pneumonia; acute fibrinous pleurisy; acute laryngitis, pharyngitis, tracheitis and bronchitis; abscess in the posterior esophageal wall; caseous and hyaline tuberculosis of bronchial, mesenteric and retroperitoneal lymph nodes; petechial hemorrhages in the mucosa of the urinary bladder; hemorrhages in the suprarenal glands; emaciation. The brain was hyperemic.

Neuropathologic Examination.—From this brain, unfortunately, only paraffin sections from the frontal and occipital lobe, the central region, the striatum, the thalamus opticus, the pons and the cerebellum were made. The sections showed definite hyperemia, all blood vessels being packed with blood corpuscles. No inflammatory changes were in the brain tissue or meninges, and there was no

increase of glia. The ganglion cells of the cortex showed postmortem changes corresponding to Nissl's water change. The cerebellar cortex was normal.

CASE 19.—*Bacillary dysentery of the mannite-fermenting group, of twenty days' duration.*

Clinical History.—A Chinese boy, aged 17 months, had had loose stools for half a month before admission, with increasing anasarca for ten days.

On admission (Jan. 30, 1932), there were severe emaciation and generalized anasarca, especially of the face, eyelids, forearms, dorsa of the hands, legs, ankles and dorsa of the feet. Examination revealed bacillary dysentery of the mannite-fermenting group, complicated by bronchopneumonia.

The condition rapidly grew worse. One day before death, purpura appeared over the skin of the arms, back and lower extremities. The child died on February 6, at 11 a. m.

Autopsy (twenty-one and three quarter hours after death).—The anatomic diagnosis was: chronic and acute ulcerative colitis (B. dysenteriae), acute mesenteric and retroperitoneal lymphadenitis, fatty change of the liver, early lobular pneumonia, edema of the lower extremities and excoriation of the skin of the anal and left inguinal regions.

Neuropathologic Examination.—Material Available: Sections from the frontal lobe, the central region, the occipital lobe and the cerebellum were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal. Throughout the cerebral cortex and all its layers there was marked water change (Nissl). The cerebellum was better preserved and showed no artificial or pathologic changes.

CASE 20.—*Bacillary dysentery of the mannite-fermenting group, of twenty days' duration.*

Clinical History.—A Chinese boy, aged 16 months, had had diarrhea, with blood and mucus, fever, vomiting and anorexia for two weeks. Marked sleepiness was also observed. The child slept a great deal of the time.

On admission, on Aug. 11, 1926, the child appeared thin, ill and dehydrated. The skin was dry and inelastic. Mentally, the boy was irritable, drowsy and dull. Tachycardia was present.

The child became increasingly toxic and weak. On August 12, almost persistent vomiting developed. On August 13, cancrum oris developed. On August 14, there was fever, and the pulse rate was increased. The heart action became weaker during the night. Death occurred on August 15, at 5:30 a. m.

Autopsy (thirty-four hours after death).—The anatomic diagnosis was: acute bacillary dysentery, with ulcerative ileocolitis; hyperplasia of mesenteric lymphatic glands; hemorrhages in the spleen, with hyalinization of the centers of malpighian bodies; fatty liver and kidneys; cancrum oris; congestion of the brain.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the central region, areas 17 and 18 and cerebellum, and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were unchanged. The cortex showed the water change (Nissl). The cerebellum was unaltered.

CASE 21.—*Bacillary dysentery of undifferentiated type, of about forty days' duration.*

Clinical History.—A Chinese girl, aged 14 months, was admitted on July 18, 1932, after having been ill for more than a month. There were severe dehydra-

tion, with a scaphoid abdomen, dry corneas, a dry, coated tongue and dry lips. The child was delirious and was irritable when touched; later she became drowsy. There were no other meningitic signs. The child died three days after admission.

Autopsy (twenty and a quarter hours after death).—The anatomic diagnosis was: bacillary dysentery, acute ulcerative colitis, bronchopneumonia, interstitial emphysema and fatty changes of the liver and kidneys.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal lobe, the central region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal. The brain tissue showed no pathologic changes, but also no gross artefacts of the ganglion cells, especially no Nissl's water change. All ganglion cells, however, were well preserved in shape and well stained; they were of the so-called "inflated" type of Fortuyn,[24] with large, clear nuclei and a rather scanty protoplasm. Besides this the cells were not distributed as densely as is usual at this age. It looked as though the intercellular substance had undergone a process of postmortem swelling. The cerebellum appeared unaltered.

CASE 22.—*Bacillary dysentery of the mannite-fermenting group, of twenty-seven days' duration.*

Clinical History.—A Chinese boy, aged 10 months, had had fever and diarrhea, with blood and mucus, for three weeks and had lost much weight.

On admission (June 18, 1926), the patient had high fever and was emaciated, pale, ill and very drowsy. However, the child seemed to be in fair condition until about twenty-four hours before death, when the temperature began to rise. He began to take feeding poorly and showed twitching of the extremities. On June 23, at 9 a. m., clonic contractions appeared in the fingers, more on the right, and in the facial muscles, especially those of the mouth. Respiration was rapid, but not labored. The heart action was rapid. At 2 p. m. on the same day cyanosis appeared; at 4 p. m. death occurred.

Autopsy (half an hour after death).—The anatomic diagnosis was: subacute ulcerative ileocolitis (B. dysenteriae); hyperplasia of ileocolic lymphatic glands; mural thrombus in the right atrium; cloudy swelling of the liver and kidneys; slight fibrosis of the spleen, with hyaline change in the germinal centers, and slight subacute focal nephritis. There were no macroscopic changes of the brain.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the central region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were unaltered. In the central region there were small and middle-sized early ischemic foci, which in single places were large enough to interrupt one whole layer (the third and the adjacent part of the second layer), but nowhere large enough to interrupt the whole cortex. Areas 17 and 18 were essentially unaltered: the architecture was primitive, and there was dense distribution of the ganglion cells. The cerebellum was unaltered.

CASE 23.—*Bacillary dysentery of the mannite-fermenting group, of about thirty-three days' duration.*

Clinical History.—A Chinese boy, aged 9 months, had had diarrhea, with mucus and pus, about eighteen days.

On admission, on June 25, 1927, the child appeared undernourished and had lost much weight and water. He was quite ill and irritable, but his mind was clear. In the following days he became increasingly weak and dehydrated. He died on July 9, 1927, at 8 a. m.

Autopsy (two days after death).—The anatomic diagnosis was: caseous tuberculosis of the left lung and tracheobronchial lymphatic glands, with tuberculous pleurisy (left) and obliteration of the left pleural cavity; tubercles in the spleen and liver; subacute ulcerative colitis (B. dysenteriae); pleural effusion (right); healing rickets. Some blood was present on the arachnoid over the left hemisphere from a blood transfusion into the sinus.

Neuropathologic Examination.—Material Available: Pyroxlin sections were made from the frontal lobe, the central region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: There was marked water change (Nissl) throughout the brain. The cerebellum was unaltered. In the meninges were some small, rare sporadic spots, which showed infiltration by round cells.

CASE 24.—*Bacillary dysentery of the mannite-fermenting group, of eighteen days' duration.*

Clinical History.—A Chinese girl, aged 6 months, was admitted on June 28, 1926, two weeks after the onset of the illness. She was extremely ill, weak and dehydrated. The skin was loose and inelastic. The abdomen was sunken. There was moderate retraction of the head. The child had lost much weight. Two days before death the abdomen became distended, and repeated vomiting occurred during the last twenty-four hours. Death took place on July 2, 1926, at 1:50 p. m.

Autopsy (three and one-half hours after death).—The anatomic diagnosis was: bacillary dysentery, with acute ulcerative ileocolitis; fatty liver; hyperplasia of the mesenteric lymph glands; rickets. The brain was without macroscopic changes.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the central region, area 17 (with area 18) and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: The meninges were normal. The blood vessels were wide and hyperemic. Throughout the cerebral cortex there was marked water change (Nissl); little more than the nuclei was visible; the protoplasm of the ganglion cells was unstained or, in some instances, only faintly stained and not sharply limited. The cerebellar cortex was unaltered.

CASE 25.—*Bacillary dysentery of the mannite-fermenting group, of five weeks' duration.*

Clinical History.—A new-born premature female Chinese baby, delivered after eight and one-half months' pregnancy, had become ill three days after birth, apparently owing to infection from the mother, who had dysentery. The baby died, with the development of extreme dehydration, after five weeks' duration of the disease. Among the final symptoms of dehydration an abnormal depression of the fontanel was noted.

Autopsy (one week after death).—The body was much emaciated and dehydrated; the skin was loose and wrinkled. The anatomic diagnosis was: prematurity, ulcerative colitis (bacillary dysentery), hyperplasia of the lymphoid

tissue of the ileum and mesenteric lymph nodes, hypoplasia of the thymus, marked emaciation and emphysema and atelectasis of the lungs. The brain appeared soft; no other macroscopic changes were observed.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made from the frontal cortex, the central region, the occipital lobe, the cerebellum and the medulla oblongata and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

Microscopic Appearance: Over all the cortex there was characteristic water change (Nissl), with round, small nuclei, perinuclear retraction space and pale, not sharply limited and, in many instances, invisible protoplasm of the ganglion cells. The cerebellum was better preserved; the superficial granular layer of the cortex was still present. The larger cells of the medulla oblongata, especially of the inferior olive, also showed water change.

FIVE CASES OF INTESTINAL TUBERCULOSIS

For comparison with the observations in dysentery, we studied the brains in twenty-eight cases of tuberculosis with intestinal impairment, most of which were cases of not only intestinal tuberculosis but also of generalized tuberculosis of the viscera. However, the intestinal symptoms were more or less dominant in all. One case was also complicated by an acute attack of cholera. From these cases, which showed essentially similar changes in the brain, which were also similar to those which we have described in dysentery, we have selected five, because they are the only ones in which Bielschowsky specimens were at our disposal. In the others we studied only pyroxylin sections stained with toluidine blue and hematoxylin-eosin and by van Gieson's method.

CASE 26.—*Far advanced chronic pulmonary tuberculosis and tuberculosis of the intestine and the omentum, complicated and exacerbated by an attack of cholera asiatica.*

Clinical History.—A Chinese man, aged 25, a soldier, had had an attack of dysentery two years before admission. He gave a history of cough, with whitish sputum, and progressive loss of weight and strength for one month. The patient had been confined to bed for one week because of weakness. Three days before admission there was a sudden onset of diarrhea and vomiting, with rapid prostration and hoarseness.

On admission (Oct. 11, 1926), there were extreme emaciation and prostration; the patient was almost in physical collapse. Mentally, he was stuporous and lethargic, although responding rationally to persistent questioning. He was extremely weak, so that it was practically impossible for him to turn in bed. His voice was weak and hoarse. The eyes were sunken and the cheek bones prominent. The skin over the extremities was cold, clammy, wet with perspiration, inelastic and coarse and over the abdomen was hot, dry and inelastic. There was evidence of marked dehydration. The finger-nails were cyanotic. The muscles were thin, wasted, weak and flabby. Respiration was slow and deep. The pulse was extremely rapid (120 a minute) and at times was almost imperceptible. The temperature was subnormal. The abdomen was retracted, scaphoid and rigid. There was clinical evidence of pulmonary tuberculosis in both lungs, with dulness over both apexes and whistling râles over the bases of both lungs, with also

the positive finding of tubercle bacilli in the sputum. There was diarrhea of "rice-water" type; cultures of stools were positive for cholera vibrios. There was vomiting of watery, greenish fluid.

After the intravenous and parenteral administration of fluids the condition of the patient improved during the following days; he became less stuporous and lethargic; vomiting became less severe, and the stools decreased in frequency and became more fecal in character on October 15. The pulse became full and strong. On October 17, however, the temperature rose; dulness over the upper lobe of the left lung increased, and on the next day this lobe was completely consolidated. Following this, the condition became worse; weakness and emaciation, in particular, became extreme, in spite of the fact that the gastrointestinal condition had improved. On October 21, a decubital ulcer developed over the left scapula. On October 26, the pulse rate became rapid (140 a minute) and weak for some time; later the cough grew worse, and the patient became nauseated. On the next day the patient became more quiet and drowsy. The pneumonic process, weakness and emaciation increased further. On November 6, roentgen examination revealed advanced tuberculosis involving the entire left lung and the upper lobe of the right lung, with practically no evidence of compensation. During the next days the condition became still worse; the temperature mounted, and the cough was severe, raising sticky, blood-tinged sputum. On November 10, the breathing was bronchial; numerous, coarse crepitant râles were heard over the entire left side of the chest. There was steadily increasing secondary anemia: on November 11, the red cell count was 2,672,000, with hemoglobin 46 per cent. After November 18, the condition became worse, with extreme weakness, profuse perspiration and pallor. The left side of the chest was flat on percussion. After November 28, the pulse was only faintly perceptible; the blood pressure was 60 systolic and 36 diastolic. Death occurred on November 29, at 12: 15 a. m. The clinical conclusion was drawn that after an attack of cholera, from which the patient had almost recovered, pulmonary tuberculosis underwent exacerbation and led to death.

Autopsy (fifteen and three quarter hours after death).—The body was greatly emaciated. The anatomic diagnosis was: chronic caseous tuberculosis of the lungs, with cavity formation and caseous pneumonia; caseous and calcified tuberculosis of tracheobronchial, mesenteric and retroperitoneal lymph nodes; ulcerative tuberculous ileocolitis and appendicitis; tubercles in the omentum, spleen, liver and kidneys; dilatation of the heart, and hyperplasia of bone marrow, with early gelatinous degeneration. The brain was macroscopically somewhat anemic, and the convolutions were perhaps a little smaller than normal. The meninges were thin and clean.

Neuropathologic Examination.—Material Available: Pyroxylin sections were made of alcohol-fixed and of formaldehyde-fixed material from the frontal lobe and the central region and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method, and frozen sections were made from formaldehyde-fixed material from the frontal lobe and the central region and were stained according to the methods of Bielschowsky and Herxheimer.

Microscopic Appearance: There were some small spots in the meninges, where numerous mononuclear cells were visible; there was no definite infiltration or tubercle formation. In the cerebral cortex were a number of sporadic small early ischemic foci, mostly perivascular. Outside these foci, most ganglion cells of the cortex appeared normal, but among them a number of pyknomorphic and even pyknotic cells, most of them clasped by glial rod and round cells, were scattered

throughout the cortex (fig. 13 *B*). The whole cortical glia appeared to be active and in a state of progressive change; numerous glial stars (ganglion cell replacements) made up of rod and round cells were seen in layers 3 to 6. In the white substance, oligodendroglial fences were present along some smaller blood vessels. Some blood vessels showed also perivascular phagocytic cells containing lipoid products of breakdown and products of breakdown which stained green by Nissl's method. The picture resembled closely that in most of our cases of dysentery, especially cases 6 and 7.

Bielschowsky specimens in this case also showed the characteristic soaking change. In one block this soaking change was developed only at the edges, while the center showed normal impregnation. In this case the same observation was made as in case 6, namely, that even in the normally stained parts of the tissue there was a certain tendency of the neurofibrils to adhere together and collect along the nucleus and the margin of the cells; many cells in these parts, however, showed a normal neurofibrillar picture.

With the hematoxylin-eosin stain and with staining by the Nissl and van Gieson methods, no postmortem change of the tissue was recognizable. The Nissl picture was entirely satisfactory. At only one place in an alcohol-fixed block did the tissue show a longitudinal hole, which could be followed through some sections up to the surface and which apparently corresponded to the canal of a blood vessel that had been torn out with a part of the pia; afterward the tissue had slightly retracted at this place.

CASE 27.—*Far advanced pulmonary tuberculosis; tuberculosis of the intestine and peritoneum.*

Clinical History.—In a Chinese girl, aged 17, the course of the disease, which was accompanied by severe emaciation, had been followed in the outpatient department since July 5, 1926, one and one-half years before death. In November, 1927, ascites and marked anasarca of the face, especially of the eyelids, and legs had developed. The patient complained also of headache and occasional double vision.

The patient was admitted on December 7. Examination revealed underdevelopment with extreme undernourishment and emaciation; the eyelids and legs were swollen, and the abdomen was distended. The girl lay flat on the bed with an apathetic facial expression. She was not interested in her surroundings. The skin was dry and hyperkeratotic over the dorsa of the hands and over the legs. There were marked pallor, general weakness and secondary anemia, with frequent stools and abdominal pain.

On the following days ascites and general anasarca increased. On December 15, a short convulsive attack with unconsciousness occurred, lasting two or three minutes. The condition became progressively worse. On December 20, at 11:30 p. m., the patient became unconscious; at the same time jerking movements of the jaws were observed. She died on December 21, at 4 p. m.

Autopsy (twenty-four hours after death).—The anatomic diagnosis was: chronic and acute caseous tuberculosis of the lungs, with conglomerate tubercles; tuberculous ulcers of the small and large intestine; caseous tuberculosis of the peritoneum, mesenteric and bronchial lymph nodes, uterus and fallopian tubes; caseous tubercles in the liver, spleen, kidneys, suprarenal gland, bone marrow of the femur and ovaries; pleural and abdominal adhesions; pleural effusion; hyperplasia of the bone marrow of the femur. The brain was anemic. The meninges were thin and clear, but did not contain tubercles; the ventricles were slightly dilated.

Neuropathologic Eamination.—Material Available: The brain was fixed in formaldehyde. Pyroxylin sections (alcohol-fixed material) were made from the frontal lobe, the central region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method; one block (from the occipital lobe) also stained with carbolfuchsin. Frozen sections were made from the frontal lobe and the cerebellum, and stained according to Bielschowsky's method.

Macroscopic Appearance: There was pseudo-atrophy of the anterior parts of the frontal lobe; here the gyri were very narrow and the sulci very wide (fig. 16 *B*).

Microscopic Appearance: In the meninges were small, sporadic places with increase of fibroblasts and mononuclear cells (lymphocytes), but no definite infiltration, no tubercle formation and no tubercle bacilli in the meninges. In the cerebral cortex were a few sporadic small early ischemic foci. Besides these, there were sporadic pyknomorphic ganglion cells scattered throughout the cortex, most of them clasped by glial cells; some glial stars were also present in layers 3 to 6. Altogether, there was less activity of the glia than in case 26. However, in this case the cortex showed some regions where activity (clasping and replacement of ganglion cells) appeared accentuated. Occasionally, there was also an increase of oligodendroglia around blood vessels in the white matter. A small number of sporadic cortical ganglion cells showed in the Nissl picture a somewhat uniform stain of the protoplasm and a perinuclear retraction space, which must be considered as a postmortem feature; no definite water change had developed, and no other postmortem changes of the cells or of the intercellular substance were present in any of the pyroxylin sections, especially in the Nissl picture.

Bielschowsky specimens showed larger and smaller areas of typical soaking change. Areas that did not show the soaking change gave an entirely normal neurofibrillar picture, without any tendency of the neurofibrils to adhere together or collect at certain parts of the cells.

The cerebellar cortex showed sporadic increase of Lannois-Paviot's layer to from five to seven rows of cells, and at rare spots small, apparently regressive shrubs were seen. Bielschowsky specimens showed a completely normal and successful impregnation of the Purkinje cells, the baskets and the supradendritic wickerwork.

Case 28.—*Tuberculosis of the intestine and peritoneum; pulmonary tuberculosis, moderately advanced.*

Clinical History.—A Russian man, aged 26, a beggar, formerly a horse dealer, had had cough for two years, with fever, hemoptysis and severe emaciation; later he also had diarrhea. He had lost much weight. At the beginning of 1926 he fell from a horse, but hurt only his body. The patient came to Peiping from Harbin in the summer of 1928 and was seen in the outpatient department on July 19, 1928. He was markedly emaciated and very ill. There was clinical evidence of pulmonary tuberculosis and plastic tuberculous peritonitis. He was transferred to the Red Cross Hospital; there inversion of sleep and delirious restlessness at night were observed. The patient slept in the day and roared from midnight till dawn, disturbing other patients.

The patient was sent back to the Peiping Union Medical College on August 1; he was now in a stuporous condition, lying on the left side with both thighs half flexed. He did not move, talk or open his mouth on request. All the reflexes were present. There were no stiffness of the neck and no Kernig sign. The

radial pulse was rapid (about 114 beats a minute) and irregular. The blood pressure was 85 systolic and 56 diastolic. There were severe emaciation, pallor, cyanosis, secondary anemia and edema of the ankles and feet. At night he roared loudly. On the next day he was drowsy, groaning aloud when touched. The pupils reacted sluggishly to light; the tendon reflexes were not obtained. The neck now appeared to be slightly rigid. On August 2, at 10:30 a. m., there was a vasomotor collapse, which was relieved by epinephrine. At noon the patient became unconscious; he died at 4:50 p. m. Circulation stopped before respiration.

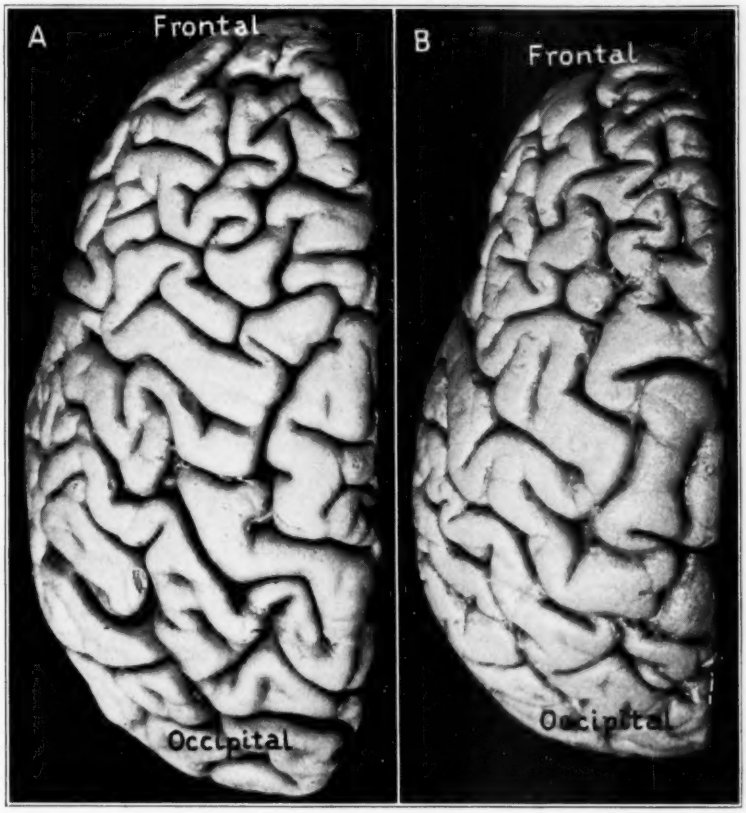


Fig. 16.—*A* (case 28), photograph of the left hemisphere of the brain from above, showing pseudo-atrophy of the frontal and occipital lobe. *B* (case 27), photograph of the left hemisphere of the brain from above, showing pseudo-atrophy of the frontal lobe.

Autopsy (twenty-four hours and forty minutes after death).—The body weighed 42.5 Kg. and measured 171 cm. Petechiae were present over the extremities. The subcutaneous fat was scanty and thin. The muscles were pale. The anatomic diagnosis was: chronic pulmonary tuberculosis, with cavity formation and caseous pneumonia; tuberculous pleuritis, with adhesions and marked thickening of pleura; tuberculosis of the bronchial lymph nodes; tuberculous enteritis and appendicitis, with ulceration; edema of the feet; decubitus; localized cystitis,

with ulceration, and localized peritonitis over the bladder. The heart was normal; and the kidneys were essentially normal. The meninges were thicker than normal, but without macroscopic signs of tuberculous meningitis. The lateral ventricles were dilated.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde; pyroxylin sections were made from the frontal cortex, the motor

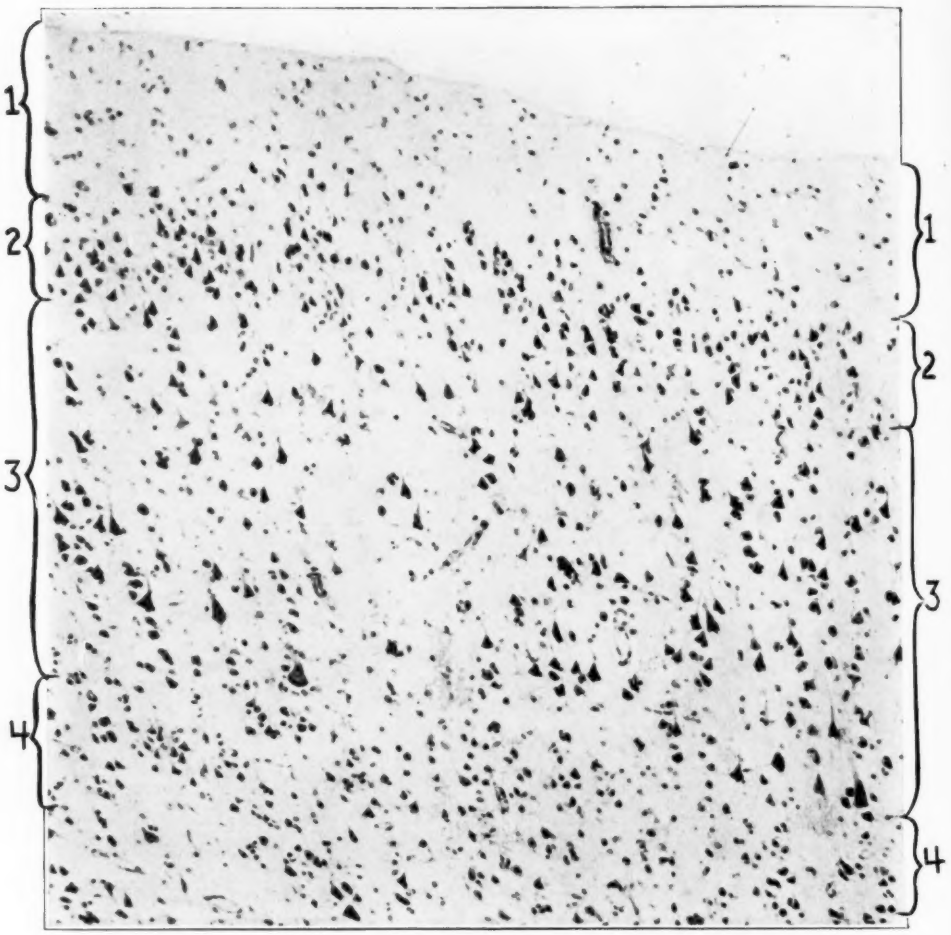


Fig. 17 (case 28).—Photomicrograph showing small early ischemic focus in the third layer of the frontal cortex. Toluidine blue stain; × 127.

region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method. Frozen sections were made from the frontal cortex and were stained according to the Bielschowsky method. In addition to these, frozen sections were made from the frontal cortex and the cerebellum and stained according to the methods of Holzer and Cajal and Globus.

Macroscopic Appearance: There was pseudo-atrophy of the frontal and the occipital lobe (fig. 16 *A*), with marked dilatation of the lateral ventricles.

Microscopic Appearance: There was fibrosis of the meninges, with no infiltration and no tubercule formation. Near one large pial vein a larger number of lymphocytes and macrophages were visible. Under a low magnification the cerebral architecture appeared almost unchanged. At a somewhat higher magnification one became aware of early small ischemic foci, which were distributed sporadically throughout the cerebral cortex (fig. 17). These foci were never large enough to destroy one whole layer at a certain spot; they were present mostly

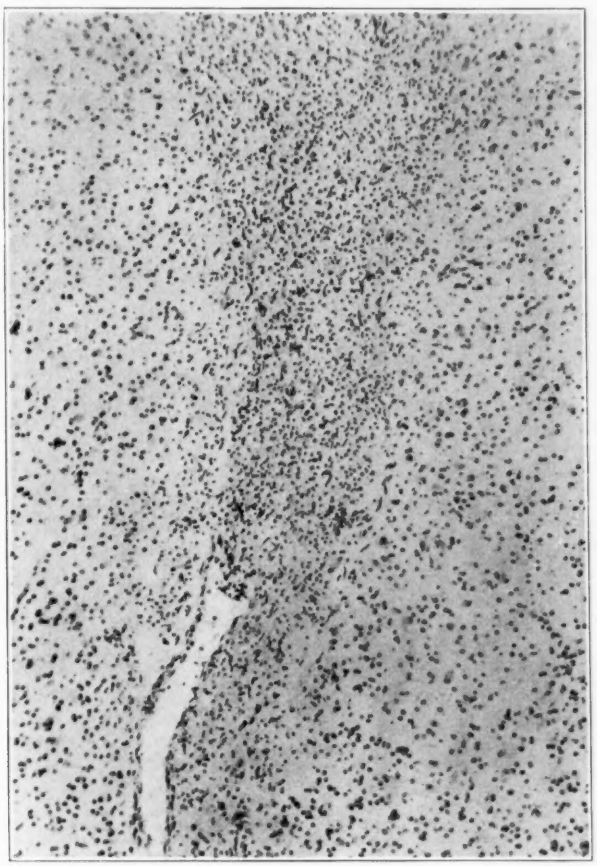


Fig. 18 (case 28).—Photomicrograph showing focus of incomplete softening in the stage of production of granular cells and big phagocytic glial elements and proliferation and new formation of endothelial elements and capillaries in the convolutional white matter of the frontal cortex. Toluidine blue stain; reduced from × 155.

in the third or the fifth layer, destroying from one third to four fifths in a radial direction and measuring about the same size in a horizontal direction. Outside these foci, sporadic pyknomorphic ganglion cells were scattered through all parts of the cortex, most of them clasped by glia cells. A number of ganglion cell replacements (glial stars) were present in layers 3 to 6. In the central parts of the

white substance of the convolutions of the frontal cortex and the central region multiple small foci of incomplete softening were present in the stage of production of granular cells and big phagocytic glial elements, with proliferation and new formation of endothelial elements and capillaries (fig. 18). These foci were rich in young cells; no scar formation was seen; they were from ten to fourteen days old and had no causal connection with the fall from the horse two years before. At other intact places in the white substance a slight increase of the oligodendroglia was present along the smaller blood vessels.

Bielschowsky specimens showed regions in which the typical soaking change had developed. Other regions showed an entirely normal neurofibrillar picture.

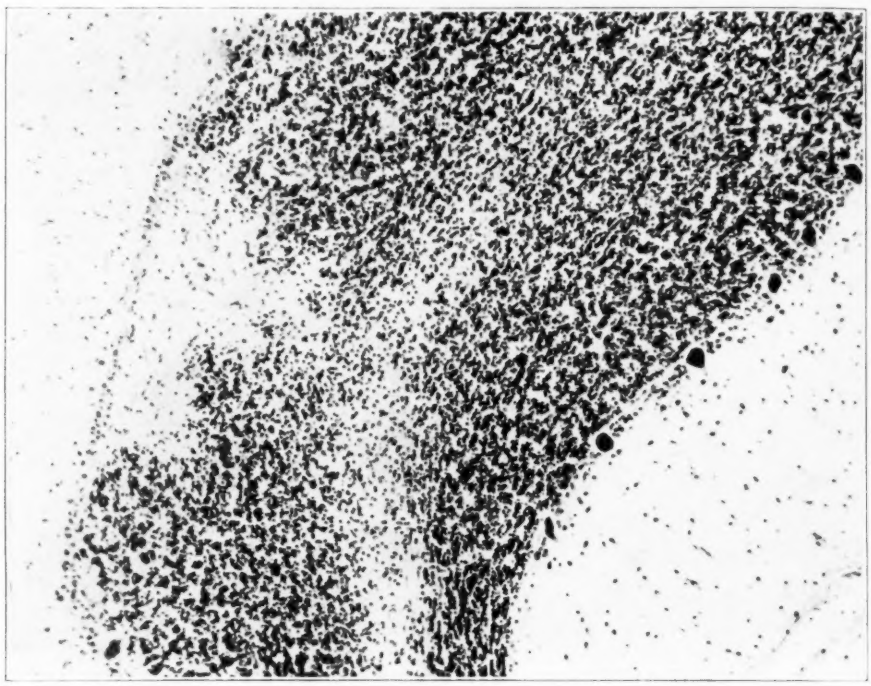


Fig. 19 (case 28).—Photomicrograph showing ischemic necrosis in the cerebellar cortex, near apex of a convolution. At the right the granular layer and the Purkinje layer are entirely normal. At the left is a big, irregularly limited necrotic defect in the granular layer. The Purkinje layer in this and the adjacent district is destroyed; all Purkinje cells here have disappeared, and only the glial layer of Lannois-Paviot is left. Toluidine blue stain; × 117.

In the cerebellum some smaller and larger foci of ischemic necrosis were present, the latter destroying parts of the Purkinje layer and the granular layer, while Lannois-Paviot's layer usually remained intact in these places (fig. 19); in only one instance in our specimens was Lannois-Paviot's layer also destroyed; in this case the focus was localized in the valley of a sulcus. In some of these foci of ischemic necrosis shadows of necrotic granular cells were still visible.

These foci may have been about six to ten days old. In other places of the cerebellar cortex some sporadic regressive glial shrubs were seen.

In specimens stained by the Nissl method there were a few cortical ganglion cells with a nucleus that was slightly too dark or a perinuclear retraction. However, the stage of preservation must in general be considered satisfactory.

This was the only case in our material in which foci of softening were present in addition to early ischemic foci.

CASE 29.—*Pulmonary tuberculosis, far advanced; hydropneumothorax; tuberculous ulcers of the small and large intestines.*

Clinical History.—A Chinese man, aged 22, a soldier, had had cough, shortness of breath and diarrhea for five months before admission and edema of the legs for one month. There had been progressive loss of appetite, weight and strength.

On admission (April 23, 1928), the patient appeared much emaciated. Mentally, he was drowsy. The face was much tanned and slightly puffy. Numerous small petechial hemorrhages were present over the skin of the chest and back. There was pitting edema over the legs, feet and hands. There was general pallor, only the face and hands being deeply pigmented.

During the next few days the condition became worse. The patient became semiconscious on April 28 in the afternoon and unconscious at 7 p. m.; he died at 9:13 p. m.

Autopsy (six days after death).—The anatomic diagnosis was: chronic and acute caseous tuberculosis of the lungs, with caseous pneumonia and cavity formation; caseous tubercles in the bronchial and mesenteric lymph nodes; rupture of a tuberculous cavity in the right lung; right pyopneumothorax; atelectasis of the right lung; fibrous pleural adhesions; tuberculous ulcers of the small and large intestines; atrophy of the heart and liver; gelatinous degeneration of the bone marrow of the femur. The pia was thin and transparent; no tubercles were present in the meninges.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde; pyroxylin sections were made from the frontal lobe, the central region, areas 17 and 18 and the cerebellum, and were stained with toluidine blue and hematoxylin-eosin and by van Gieson's method. Frozen sections were made from the frontal lobe and were stained according to the method of Bielschowsky and Herxheimer.

Macroscopic Appearance: There was no pseudo-atrophy and no dilatation of the ventricles.

Microscopic Appearance: The meninges were unchanged. In the cerebral cortex were small ischemic foci and scattered pyknomorphic cells with their pericellular glial rosettes, as well as a replacement of ganglion cells. However, in this case many normal as well as pathologic cells had undergone definite postmortem change: They showed marked perinuclear retraction spaces and, in many instances, vacuolation of the pale protoplasm. The Bielschowsky specimens showed regions in which the typical soaking change had developed. But there were also regions in which the neurofibrillar impregnation was entirely normal or, in some instances, normal but somewhat pale. It is interesting that here also in places that showed normal or only slightly pale neurofibrillar impregnation some of the nuclei of the ganglion cells and of the neighboring glial elements showed a tendency to stain a brownish shade similar to that of the neurofibrils. The cere-

bellum showed increase of Lannois-Paviot's layer to from eight to ten rows of cells in some places, especially in the environs of damaged Purkinje cells, but no definite shrub formation.

CASE 30.—*Pulmonary tuberculosis, far advanced, with tuberculosis of the intestine.*

Clinical History.—A Chinese man, aged 23, a soldier, had had cough, fever, abdominal pain and diarrhea for about two months.

On admission (June 19, 1928), there was extreme emaciation. The pulse was almost imperceptible. The eyes were sunken; the abdomen was scaphoid, and there was marked prostration. Mentally, the patient was slightly dull. The skin was dry and ashen. There were secondary anemia, and a rapid and feeble pulse (124 a minute). The blood pressure was 76 systolic and 50 diastolic. Death occurred on June 22, 1928.

Autopsy (five days after death).—The body was greatly emaciated; it weighed 33.6 Kg. and measured 166 cm. The anatomic diagnosis was: acute caseous pulmonary tuberculosis, with cavity formation; caseous pneumonia; caseous tuberculosis of the bronchial lymph nodes; dilatation of the heart; pleural effusion and adhesions; hydropericardium; peritoneal adhesions; infarcts of the spleen and kidneys; decubitus ulcers; ulcers of the ileum and colon; gelatinous degeneration of the bone marrow of the femur. The brain was anemic.

Neuropathologic Examination.—Material Available: The brain was fixed in formaldehyde; pyroxylin sections were made from the frontal lobe, the motor region, areas 17 and 18 and the cerebellum and were stained with toluidine blue and hemaxtoyin-eosin and by van Gieson's method. Frozen sections ware made from the frontal lobe and stained according to the methods of Bielschowsky and Herxheimer.

Macroscopic Appearance: There was no pseudo-atrophy or dilatation of the ventricles.

Microscopic Appearance: The meninges were free from pathologic changes. The cerebral cortex showed sporadic small early ischemic foci. Outside these foci, in layers 3 to 6, were a number of scattered pyknomorphic and even pyknotic cells, clasped by glia cells; the number of complete ganglion cell replacements was smaller in this case than in others. The Nissl picture was, on the whole, astonishingly well preserved, if one considers the long time between death and fixation. However, the sections showed definite postmortem changes: In the central parts of the white matter of the convolutions round holes were visible, due to putrefaction; a number of ganglion cells, scattered throughout the cortex, showed perinuclear retraction spaces and vacuolation. Stains for fat revealed small amounts of lipoid in sporadic ganglion cells and in adventitial elements of some blood vessels.

The Bielschowsky specimens showed regions in which the soaking change had developed to a certain extent. Nonargentophilic regions presented also a much altered appearance when stained by the Bielschowsky method. They were brownish, and the nuclei stood out in a somewhat darker brownish shade, while the neurofibrils were adherent together, forming crumbled, indistinct masses, especially along the margins of the cells, or had entirely disappeared.

In the cerebellum some postmortem holes due to putrefaction were seen. In the intact parts there was an increase of Lannois-Paviot's layer to from five to seven rows of cells at some places, but no shrub formation.

COMMENT

The chief fact that impressed us in studying these cases of intestinal infections with terminal cachexia and lethal outcome was the great similarity in the cliniconeuropsychiatric, somatic and neuro-anatomic features, in spite of the differing etiology: amebic dysentery, bacillary dysentery of the mannite-fermenting group, bacillary dysentery of the Shiga type and intestinal tuberculosis, which in one case was combined with Asiatic cholera.

The neuropsychiatric symptoms presented in our cases were: drowsiness; mental dulness and cloudiness; stupor; apathetic and lethargic conditions; irritable, irrational and delirious conditions; psychomotor excitement; convulsions, with unconsciousness in two cases (8 and *27*), which is a rather rare occurrence in adults; jacksonian-like attacks in a child (case *22*); headache; impairment of hearing; vertigo; double vision; areflexia; insomnia; sleepiness; inversion of sleep; listlessness; disinterested behavior, and loss of spontaneous activity. Unfortunately, in the cases that came to autopsy the patients had not been subjected to special and more detailed psychiatric examinations, which might have revealed more about the special symptomatology.

The general somatic signs—general weakness, emaciation, dehydration, exhaustion, prostration, secondary anemia, nutritional edema, xerodermia, xerophthalmia, keratomalacia and cachectic cutaneous purpura—all indicated cachexia.

The neuro-anatomic changes may be divided into different groups, which we shall present according to Spielmeyer's classification. Spielmeyer [3b] divided the histopathologic changes in infectious diseases into three groups: (1) regressive parenchymal changes, (2) circulatory changes and (3) inflammatory changes.

In the cases of dysentery only the first two of these groups were represented; inflammatory changes were entirely absent in the brains in our cases. This is of interest because it differs from the results of experiments on animals, but it may be due to the relatively small amount of material.

Circulatory changes, however, are common; they were evident not only in nearly all the cases of dysentery, but also in almost all the cases of intestinal tuberculosis. They occurred in various degrees and forms. In most of our cases there were sporadic small ischemic [25] foci in the gray matter of the cerebral cortex (figs. 2, 8 and 17). The site of

25. The short term "ischemic" is used by us with the meaning of sequestration from the streaming blood in the sense of Ricker (Die Wiederbelebung des anatomischen Präparats; ein Programm für neurologische Arbeit, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:529, 1928). We are conscious of the fact that not only ischemia but stasis as well may cause such foci.

predilection was the third and the fifth layer of the gray matter. The size varied from one third to four fifths of the breadth of one of these layers in a radial direction and about the same in a horizontal direction. In only one case (*22*) did they reach the breadth of the whole third layer, even penetrating into the second, thus interrupting the whole breadth of the third layer; in one other case complicated with arteriosclerosis (case 11) such a focus interrupted the whole cortical ribbon at one place. These cases, however, were exceptions; most of the foci were small.

The foci of circulatory change were similar in histologic appearance. Most of them were obviously located in the environs of smaller cortical blood vessels. The foci were characterized by deficiency of a relatively large number of the local ganglion cells. Some of these were replaced by small glial stars, while the majority had disappeared without leaving recognizable traces. The few remaining ganglion cells showed without exception severe changes of various types.

Figure 9 is a photomicrograph under higher magnification of part of an ischemic focus, taken from figure 8, in the third layer of the frontal cortex in case 7 (bacillary dysentery of the mannite-fermenting group). In the immediate neighborhood of the small blood vessel is a monster glia cell, such as is frequently observed in or near circulatory foci or at other places where nerve tissue is destroyed. Furthermore, to the right in this picture are three severely altered ganglion cells. The left upper cell is pyknotic. At the place of its apical dendrite is a glial rod cell, which is clasping or already replacing the apical dendrite; another glial cell, with a round nucleus, is clasping the cell body. At the right of this cell is a pale cell, almost a shadow cell, with some few overimpregnated dots in it. But the most severely damaged cell is the third cell, that in the inferior half of the picture, under the pyknotic cell. Of this cell, which has undergone an acute process of colliquefaction and expulsion of the nucleus with karyorrhexis, only ruins are visible. The distal part of the apical dendrite is still visible, and at the other side of the cell body one can recognize a remnant of the broken nucleus, namely, the nucleolus of the ganglion cell and a half moon-shaped segment of the overimpregnated and thickened nuclear membrane. The body of this cell is replaced by three glial cells with round nuclei. Some of their thin processes, showing small stipplings, are also recognizable in the Nissl picture. However, these are not the only type of ganglion cell changes to be seen in the ischemic foci of the cortex; in many instances one observes shadow cells (fig. 13, from case 9) and typical ischemic cells. Figure 10 *A* (from case 7) shows an ischemic cell from the margin of an ischemic focus, with a characteristic dark nucleus and pale protoplasm; the apical dendrite is just melting off and is still connected

with the cell body by only a small strip of protoplasm. Finally, the cells disappear or become replaced by glial stars. Figure 10 *B*, from case 7, shows such a glial star from the edge of an ischemic focus. None of the cases showed fully developed foci of softening, with melting of the tissue, in the gray cortical substance.

Similar small deficiencies or "gaps" in the gray matter were described by Schröder [26] in cases of symptomatic psychosis in typhoid fever and pneumonia. Husler and Spatz [27] described similar and also larger foci of this kind in whooping cough. In typhoid fever, however, and in dysentery Husler and Spatz observed those foci only rarely and in addition saw signs of diffuse cell deficiency of only slight degree. Schröder, as well as Husler and Spatz, originally considered these foci as "toxic" in origin; but the excellent descriptions of these authors make it easy to recognize them as circulatory according to present knowledge, especially according to the findings of Bodechtel and Müller,[28] Müller [29] and Bodechtel.[4]

In the white matter in our cases that we had opportunity to study with myelin sheath stains, we also observed similar early small perivascular ischemic foci (fig. 12) such as have already been described by Spielmeyer.[3b] In only one case (case 28, intestinal tuberculosis, fig. 18) did we see multiple foci of softening in the white matter of the cortex in the stage of production of glial elements and capillaries. We saw many glial granular cells and big phagocytic glia cells, but here also the tissue had not yet undergone dissolution.

In the cerebellar cortex in a number of cases there were damage to Purkinje cells and the formation of glial shrubs; in many cases, however, there was only a certain productive activity of Lannois-Paviot's layer, without actual shrub formation. All these changes in the cerebellar cortex must be considered also as vascular in origin according to recent studies in Spielmeyer's laboratory (Scherer,[17] Bodechtel [4a] and others). In only one case were there also foci of complete ischemic necrosis in the cerebellar cortex, with focal destruction of the granular layer and the Purkinje cells, only Lannois-Paviot's glial layer being

26. Schröder, P.: Anatomische Befunde bei einigen Fällen von akuten Psychosen, Allg. Ztschr. f. Psychiat. **66**:203, 1909.

27. Husler, J., and Spatz, H.: Die "Keuchhusten-Eklampsie," Ztschr. f. Kinderh. **38**:428, 1924.

28. Bodechtel, G., and Müller, G.: Die geweblichen Veränderungen bei der experimentellen Gehirnembolie, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**:764, 1930.

29. Müller, G.: Zur Frage der Altersbestimmung histologischer Veränderungen im menschlichen Gehirn unter Berücksichtigung der örtlichen Verteilung, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**: 1, 1930.

left intact in these places (fig. 19), in a manner similar to that demonstrated by Bériel [30] for such vascular lesions in the cerebellar cortex.

The blood vessels themselves were essentially unaltered in our cases, with the exception of two, in one of which the condition was complicated by arteriosclerosis and chronic nephritis (case 11), and in the other by atrophic cirrhosis of the liver and ancylostomiasis (case 15). No hemorrhages, especially no annular hemorrhages, were seen. In many cases some blood vessels contained lipoid products of breakdown; others had substances that stained green with toluidine blue (probably partially iron) in phagocytic perivascular cells (fig. 15).

A point of interest is the determination of the age of the different circulatory foci in these cases. According to present knowledge, the ischemic foci in the gray matter were only a few hours or one or a few days old. The same is true for the small perivascular disintegrations in the white matter of the cortical convolutions and for most of the circulatory changes in the cerebellar cortex. Only the foci of softening in the white matter of the cerebral cortex and the foci of ischemic necrosis in the cerebellum, which we found in only one case (case 28, intestinal tuberculosis) were older; these may have been from 6 to 14 days old. It is of interest that this is also the only case in which the patient was delirious for a considerable period before death, namely, one week. Thus, a coincidence in the probable time of development of the multiple foci of softening and the time of occurrence of delirious manifestations in the clinical picture is evident in this case. In all other cases we observed only ischemic foci which were a few hours, one day, or, at most, a few days old. In some cases also the development of these foci found its expression in the clinical picture. We do not hesitate to consider them as the anatomic substrate of, for instance, the jacksonian-like attacks which occurred in case 22 on the day of death, the psychomotor excitement that occurred in case 17 on the day of death, or the convulsions in which the patient in case 8 died. In many other cases, however, they did not cause noticeable clinical symptoms; such symptoms may have been masked in the general picture of the terminal cachexia or even in the death agony. However, the presence of fresh ischemic foci is also of clinical interest in these cases, as they indicate the ultimate cause of death and allow us to state definitely with more certainty than we would be allowed to do by judging from the observations at autopsy on any other organ that our patients died from circulatory failure.

Another group of anatomic changes observed in our cases is not circulatory in nature, but belongs in the group of regressive parenchymal

30. Bériel, L.: Die sogenannte "äussere Körnerschicht" (Vogt und Astwazaturow) in akquirierten Kleinhirnerkrankungen, Arch. f. Psychiat. **51**: 1080, 1913.

changes. By this we mean the sporadic disseminated pyknomorphic [31] and even pyknotic cells which we observed outside of the ischemic foci, scattered throughout the gray matter of the cerebral cortex in most cases. Most of them were clasped by glial elements—glial rod and round cells. Figure 3 *A* shows such a pyknomorphic clasped ganglion cell from the third layer of the precentral region in case 6 (amebic dysentery), and figure 3 *B* shows one from the fifth layer of the frontal cortex in case 26 (intestinal tuberculosis). In these cases also a number of sporadic cells were already destroyed and replaced by glial stars (ganglion cell replacements). The pyknomorphic clasped cells and the ganglion cell replacements accumulated in some cases at certain places. Figure 14 shows part of the third layer of the frontal cortex in case 9 (bacillary dysentery of the mannite-fermenting group); it is especially rich in pyknomorphic clasped cells and ganglion cell replacements at certain places. Our material is too limited, however, and in most cases not enough different areas could be examined to determine the distribution of this change. However, cases that showed local accentuation of this change, the pyknomorphic clasped cells and the ganglion cell replacements could also be found sporadically throughout the other places examined in the cortex. No area was entirely free from it. Concerning the localization in cortical strata, the change occurred in most instances about equally markedly in layers 3 to 6. Only in some instances did the deeper layers seem to be favored; the change was always present also in the third layer.

These regressive parenchymatous changes in the cortex, represented by sporadic pyknomorphism and pyknotism and sporadic deficiency of ganglion cells, were accompanied not only by a pericellular progressive reaction of the neuroglia in the gray matter itself, which formed rosettes and stars, clasping and replacing ganglion cells, but also by an independent perivascular progressive reaction of the glia, which was especially marked in the white substance of the convolutions, where in many instances perivascular glial nodules and glial rims were seen (fig. 4).

The changes of this group, which we shall call for the sake of simplicity the "group of scattered parenchymatous and glial changes," have been described in the literature in different chronic and acute systemic disorders. Miyake [32] described perivascular and glial foci (which, however, he did not recognize as glial) in different systemic diseases, among them tuberculous peritonitis and typhoid fever. Rezza [33]

31. The pyknomorphism of ganglion cells has been previously regarded as an artefact by Nissl. Recent studies of Müller (footnote 29) demonstrated this type of pyknomorphic cells as pathologic (pages 56, 66 and 99).

32. Miyake, Koichi: Beitrag zur Kenntnis der Altersveränderungen der menschlichen Hirnrinde, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **13**: 212, 1906.

33. Rezza, A.: Beitrag zur pathologischen Anatomie der Pellagrapsychosen, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**: 1, 1912.

described the coincidence of shrinking of ganglion cells, pericellular glial rosettes and perivascular glial rims in pellagra. Kirschbaum [34] described various ganglion cell changes with pericellular glial increase and perivascular glial knots in the white substance in cases of more or less generalized tuberculosis with tuberculous meningitis, but independent of the direct tuberculous lesions in the brain. Scholz [35] described small glial foci, rosettes, stars and perivascular knots and rims as frequent in infectious and toxic systemic diseases. Oesterlin [15] described glial knots and ganglion cell replacements in different infectious diseases and also in pernicious anemia and hemorrhagic diathesis. Rasdolsky [36] described perivascular proliferation of glia in thyroidectomized animals. Hinrichs [37] observed production of perivascular glial rims in a case of miliary tuberculosis and considered them as toxic in origin. Jakob,[38] in discussing Hinrichs' communication, mentioned their occurrence in cachetic conditions and in pernicious anemia. Bodechtel [4b] noted perivascular glial knots and rims in uremia, which he considered as toxic in origin. Müller [29] observed perivascular increase of glia in the brain of a patient who survived carbon monoxide poisoning for from forty-nine to fifty-nine hours, and pyknomorphism of ganglion cells, with the formation of glial rosettes and ganglion cell replacements in the case of a patient who survived secondary butyl β bromallyl barbituric and ether anesthesia for three hours.[39] But Müller emphasized that these represent only the earliest periods within which these changes may develop and do not exclude the possibility that the same change may develop later in other cases or may persist longer. Here the intensity of the damaging agent is of importance: A less intensive agent may cause the same change within a greater length of time.

Therefore, one sees that the data in the literature furnish many examples of the occurrence of such disseminated parenchymatous and glial changes, but no information as to their ultimate etiology and no standards for determining the time of their development. Most authors consider them as toxic, but toxic is merely a useful term which does

---

34. Kirschbaum, W.: Ueber die Tuberkulose des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **66:** 283, 1921.

35. Scholz, W.: Ueber herdförmige, protoplasmatische Gliawucherungen von syncytialem Charakter, Ztschr. f. d. ges. Neurol. u. Psychiat. **79:** 114, 1922.

36. Rasdolsky, J.: Histologische Veränderungen in dem zentralen und peripherischen Nervensystem der Tiere mit exstirpierten Schild- und Nebenschilddrüsen, Ztschr. f. d. ges. Neurol. u. Psychiat. **106:** 96, 1926.

37. Hinrichs, U.: Ueber einen besonderen Hirnbefund bei Miliartuberkulose, Deutsche Ztschr. f. Nervenh. **117:**119, 1931; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **60:**447, 1931.

38. Jakob, A.: Discussion, in Ges. d. Neurol. u. Psychiat. Gross-Hamburgs gemeinsam mit. d. Ver. Norddtsch. Neurol. u. Psych. 18-19, October 1930; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **60:**447, 1931.

39. Müller,[29] p. 78, fig. 32.

not imply anything definite about the mechanism of the biologic and the physicochemical processes that are the ultimate cause of the pathologic change. Recently, the term toxic has begun to be resolved into its radicals. Spielmeyer and his school, especially Bodechtel, successfully isolated a circulatory component. But what is left is still complex and unsolved. Clinical and physiologic advances have been much greater than anatomic advances. The importance of avitaminotic components, which are the binding link from the toxic to the cachectic conditions is known, but the anatomy of avitaminosis in the brain is still lacking. The physiologic importance of changes in permeability in toxic conditions is known, especially since Stern's [40] experiments, but anatomically these changes are not yet comprehensible.

The data in the literature cited also give no standards for determining the age of the scattered or disseminated parenchymatous and glial changes in our cases. However, among our cases they were present only in conditions of rather long duration; they were absent in the acute cases (8 and 17, bacillary dysentery of the Shiga type). However, this may be due not so much to the duration of the diseases as to the severity of the terminal cachectic condition, which needs for its full development a certain length of time and therefore develops only in cases of longer duration.

As we do not know the time of development of these disseminated parenchymatous and glial changes, we are unable at present to state anything about their clinical importance. Here some interesting questions arise: 1. Are these changes older than the ultimate circulatory failure that causes the ischemic foci? 2. Have the changes anything to do with the cachexia or the avitaminosis, and are they to a certain extent parallel to the degenerative changes in the eyes and the skin which were present in many of our cases? 3. Are they recognizable in the clinical neuropsychiatric picture? 4. Are they a mere inactive part in the pathologic picture of the disease, or may they play an active rôle in the pernicious course and the fatal outcome of the disease by contributing to the circulatory failure through the vasomotor system, circulatory failure being undoubtedly the ultimate cause of death in our cases of dysentery? Further study and inquiry into these questions might reveal some points of no small interest.

Two more anatomic features in the cases cannot be explained satisfactorily at this time. One is the macroscopic condition, which we described as pseudo-atrophy. By this we mean the occurrence of narrow convolutions and wide sulci, especially in the frontal lobe, in dysentery as well as in intestinal tuberculosis (in cases without meningitis and

40. Stern, L.: Les dernières recherches concernant le fonctionnement de la barrière hémato-encéphalique, Schweiz. med. Wchnschr. **59**: 935, 1929

also in those without meningofibrosis), sometimes associated with slight dilatation of the ventricles. This pseudo-atrophy was present in five cases (*6*, *7*, *26*, *27* and *28*), being associated in two of them (*27* and *28*) with dilatation of the ventricles. In one case (13) only dilatation of the ventricles was noted.

All that we are able to state is that this atrophic appearance cannot be caused by the early ischemic foci (which had not yet caused dissolution of tissue substance) and also not by the slight disseminated parenchymatous change, which was not severe enough to cause any gross alteration, especially disarrangement of the cortical architecture. Therefore, some unknown substance, in addition to the ganglion cells, must have been altered in these brains. A certain amount of probability exists to our minds that dehydration may play a rôle in the production of this "emaciation" or pseudo-atrophy of the brain. The fact that in severely dehydrated children depression of the fontanel may be noted, as in case *25*, points in this direction. Similar pseudo-atrophic conditions of the brain, even proved by measurement of the difference between the capacity of the skull and the weight of the brain, were described by Apelt [41] in systemic diseases with a chronic course and general cachexia. Apelt considered this to be a decrease of "brain mass," but gave no further specification in detail. Recently, "atrophy" of the brain, especially of the frontal lobes, was reported in pellagra by Wyjasnowsky.[42] We are inclined to consider this also as a pseudo-atrophy in line with the observations in our cases of dysentery and tuberculosis.

The next point that we are unable to explain at present is the tendency of all the cases in our material that we could examine with Bielschowsky's silver method to present alterations in the neurofibrillar picture, which we have described as soaking change. The occurrence of neurofibrillar alterations is of interest because one finds it described in the literature in similar conditions: by Chanutina [43] and Michailow [44] in cholera; by Rezza [33] in pellagra; by Donaggio [45] in animals that

41. Apelt, F.: Der Wert von Schädelkapazitätsmessungen und vergleichenden Hirngewichtsbestimmungen für die innere Medizin und die Neurologie, Deutsche Ztschr. f. Nervenh. **35:** 306, 1908.

42. Wyjasnowsky, A. J.: Ueber Pellagra-Psychosen (klinische Bemerkungen und Beobachtungen), Ztschr. f. d. ges. Neurol. u. Psychiat. **144:** 338, 1933.

43. Chanutina: Zur Frage der Veränderungen des Rückenmarks bei der Cholera, Russk. vrach. **34** and **35**, 1909.

44. Michailow, S.: Pathologisch-anatomische Untersuchungen der feineren Struktur der Gehirnrinde, der Rinde des Kleinhirns, des verlängerten und des Rückenmarks des Menschen bei asiatischer Cholera, Arch. f. Psychiat. **51:** 587, 1913.

45. Donaggio, A.: Effetti dell azione combinata del digiuno e del freddo sui centri nervosi di mammiferi adulti, Riv. sper. di freniat. **32:** 373, 1906.

had been starved and frozen to death and by Lewy [46] and Rasdolsky [36] in cachexia thyreopriva. We observed alterations in the neurofibrillar impregnation in nine cases: case 6 (chronic amebic dysentery), case 7 (chronic bacillary dysentery of the mannite-fermenting group), case 8 (acute bacillary dysentery of the Shiga type), case 9 (chronic bacillary dysentery of the mannite-fermenting group), case 26 (intestinal tuberculosis complicated by cholera) and cases 27, 28, 29 and 30 (intestinal tuberculosis). All those cases presented at some places the soaking change of neurofibrils—that is, argentophilia, thickening, formation of more or less winding strands and crumbling or disappearance of the intracellular neurofibrils, associated with argentophilia of the nuclei of nerve and glial cells (figs. 5 and 11), while at other places the Bielschowsky picture appeared to be entirely normal or in some cases showed only a slight tendency of the neurofibrils to adhere together or collect along the nucleus or the margin of the cell in some instances (figs. 6 and 7). This soaking change of neurofibrils, as we have called it, has a marked resemblance to the artificial change that was produced experimentally by one of us (Alexander) by soaking fresh brain tissue in distilled water or saline solutions. The argentophilia of the nuclei is especially characteristic in both conditions. More detailed statements regarding this neurofibrillar change are given in a special study.[23] There it is pointed out that at least one component in the production of this neurofibrillar alteration is artificial (post mortem), but here also a fully satisfactory explanation must be left for further study.

SUMMARY

The anatomic changes in the brains in twenty-five cases of gastrointestinal infection with terminal cachexia have been described. Among them were twenty cases of dysentery of different types (four cases of amebic dysentery, thirteen of bacillary dysentery of the mannite-fermenting group, two of bacillary dysentery of the Shiga type and one of undifferentiated bacillary dysentery) and five cases of intestinal tuberculosis, one of which was complicated by Asiatic cholera.

The following kinds of anatomic alterations were found:

(1) Circulatory foci, which were only a few hours, a day or a few days old and indicated circulatory failure as the ultimate cause of death in these cases. The probable age of these foci corresponded with the time of occurrence of certain clinical symptoms which made their appearance at varying short periods before death: convulsions, jacksonian-like attacks, psychomotor excitement and, in one case, a delirious condition.

46. Lewy, F. H. in Alzheimer, A., and Lewandowsky, M.: Die Lehre vom Tonus und der Bewegung, Monographie aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1923, no. 34.

(2) Disseminated parenchymatous and glial changes, such as pyknomorphism, pyknotism and destruction of cortical ganglion cells, associated with progressive changes of the neuroglia, which clasped ganglion cells, replaced them and formed perivascular glial rims and knots. The ultimate etiology and the age of these lesions could not be determined. They seemed to have a certain relationship to the duration of the disease and the severity of the cachectic condition.

(3) In addition, a peculiar alteration of the macroscopic appearance (pseudo-atrophy) of the brains in some cases was observed. This cannot be explained by the small early ischemic foci or the slight disseminated parenchymatous damage alone. Its possible relationship to dehydration is discussed.

(4) A certain tendency of the tissue to give rise to an alteration in Bielschowsky's silver impregnation of the neurofibrils, which can be produced experimentally by soaking fresh normal brain tissue in distilled water or saline solutions (soaking change). Its exact nature and the significance of its occurrence need further study.

CHANGES IN THE CEREBRAL CORTEX PRODUCED BY THERMOCOAGULATION

A SUGGESTION TO NEUROSURGERY

J. G. DUSSER DE BARENNE, M.D.
AND
H. M. ZIMMERMAN, M.D.
NEW HAVEN, CONN.

Recently the method of laminar thermocoagulation has been described [1] as a method of approach to the physiology of the various layers of the cerebral cortex.

It was established that local application of moderate heat for short periods to the exposed surface of the cortex results in destruction of its nerve elements. "Dosing" the heat applied allows the limitation at will of the depth of the lesion to any number of consecutive cortical layers. Thus, application of 65 C. for two seconds destroys the two superficial layers, 70 C. for three seconds, the three outer layers, and 70 C. for four seconds, the four outer layers; application of 80 C. for five seconds destroys all the layers.

For a description of the technic and of the necessary simple equipment we refer the reader to the papers already published.[1] In this communication we shall discuss the pathologic observations, especially some new observations on the chronic stages and the effect of lower temperature.

The typical picture of a lesion produced in the monkey by thermocoagulation at 80.C., extending through the whole thickness of the cortex and after a survival period of seven days, is given in figure 1.

The lesion is sharply outlined by a definite wall of proliferating glia and fibroblasts. It extends through all the cortical laminae into the white matter, but the surface of the cortex is unbroken. All the nerve cells in

---

From the Laboratory of Neurophysiology and the Department of Pathology, Yale University.

1. Dusser de Barenne, J. G.: Laminar Destruction of the Nerve Cells of the Cerebral Cortex, Science **77**:546 (June 2) 1933; Selektive Abtötung der Nervenzellschichten der Grosshirnrinde; Die Methode der laminären Thermocoagulation der Rinde, with addendum by H. M. Zimmerman on the pathologic findings, Ztschr. f. d. ges. Neurol. u. Psychiat. **147**:280, 1933; Welche Elemente der Grosshirnrinde bringen bei ihrer elektrischen Reizung die motorischen Reaktionen hervor? Arch. f. d. ges. Physiol. **233**:529, 1933; The Origin of the Motor Reactions Produced by Electrical Stimulation of the Cerebral Cortex, Arch. Neurol. & Psychiat. **31**:1129 (June) 1934.

the heated zone have disappeared, but the glia, which is arranged in the usual laminar manner, is still present and is well stained. This is in contrast to the state of the glia in the "chronic" experiments which will be described later. Increased numbers of astrocytes and microglia lie beyond the wall which delimits the lesion; the ganglion cells just outside the glial-fibroblastic wall are in an excellent state of preservation.

Figure 2 shows the cortex of a monkey heated at 65 C. for three seconds, which has resulted in the destruction of the two superficial layers and the outer portion of the third layer. The survival period in this experiment was again seven days, and it is seen that all the nerve cells in the devastated outer layers have disappeared, a state which was

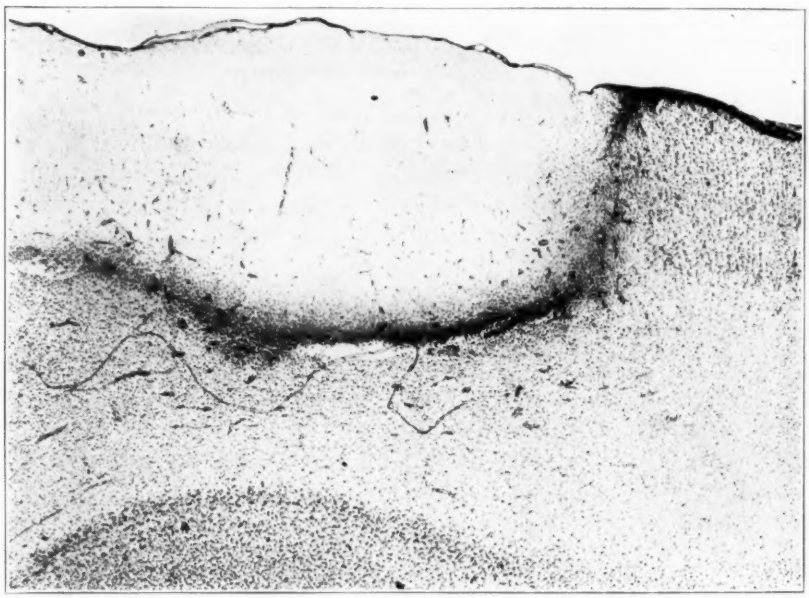


Fig. 1.—A photomicrograph showing a lesion produced in the parietal cortex of a monkey by thermocoagulation at 80 C. for six seconds. The survival period was seven days. Nissl stain; magnification, × 15.

found to exist within thirty-six hours. Even in "acute" experiments in which the animal is killed one or two hours after thermocoagulation, it can be seen that some of the killed nerve cells have already disappeared. In experiments with such short survival periods, there are frequently found within the heated region small, irregularly shaped areas in which fewer nerve cells are present than normally. This indicates that within one or two hours after thermocoagulation cytolytic changes lead to disintegration and dissolution of some of the nerve cells, a process which is completed, so far as the nerve cells in the heated area are concerned, within thirty-six hours.

In some experiments we have tried to determine whether heating the cortex at a lower temperature, though one still above the normal body temperature, results in death of the nerve cells. It was found that the application of 50 C. for half a minute results in the death of the nerve cells of the superficial layers. As this period of application is much longer than that necessary to kill the cortical layers at higher temperatures (from 65 to 80 C.), it might be possible that the death of the nerve cells was due not to the heat but more to the compression of the cortex for half a minute by the weight of the heating apparatus. Although this weighs but 26 Gm., its weight might be enough, when applied for half a minute, to produce a local ischemia of the cortex, and through that factor to produce an injury to the nerve cells and their subsequent death.

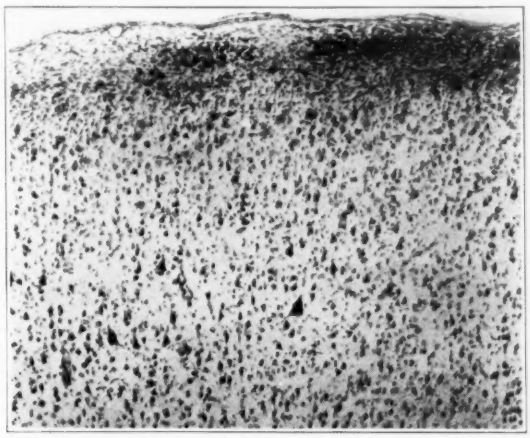


Fig. 2.—A photomicrograph showing destruction of the two outer layers and the superficial part of the third layer of the motor cortex of a monkey by thermocoagulation at 65 C. for three seconds. The survival period was seven days. Nissl stain; magnification, × 60.

The microscopic picture of the cortical lesion resulting from thermocoagulation at 50 C. is quite different from that obtained after thermocoagulation at 80 C. It shows a complete loss of the ganglion cells of the second layer and of the superficial part of the third layer (fig. 3). The first layer, of course, is also destroyed. All the involved laminae contain a marked glial and fibroblastic proliferative response, corresponding to that seen in the "wall" of the lesions produced with the higher temperatures (fig. 1). Most of the large pyramidal cells of the deeper part of the third layer are intact, as are also the cells in the fourth and fifth layers of the motor cortex.

To decide whether the pressure of the heating apparatus as such resulted in injury to the cortex, we applied the unheated apparatus for sixty seconds to the cortex.

Figure 4 shows the normal appearance of the motor cortex of the same animal from which the preparation shown in figure 3 was obtained. The heated and unheated areas in this animal were immediately adjacent. Thus it can be asserted that the pressure exerted by the heating apparatus, even when applied for one minute, does not produce the cortical lesions. The essential factor is the heating of the cortex.

The fact that application of heat at 50 C. for half a minute results in death of the nerve cells of the superficial cortical layers is, of course, interesting from the point of view of general neuropathology. It should be emphasized, however, that the use of such low temperatures is not

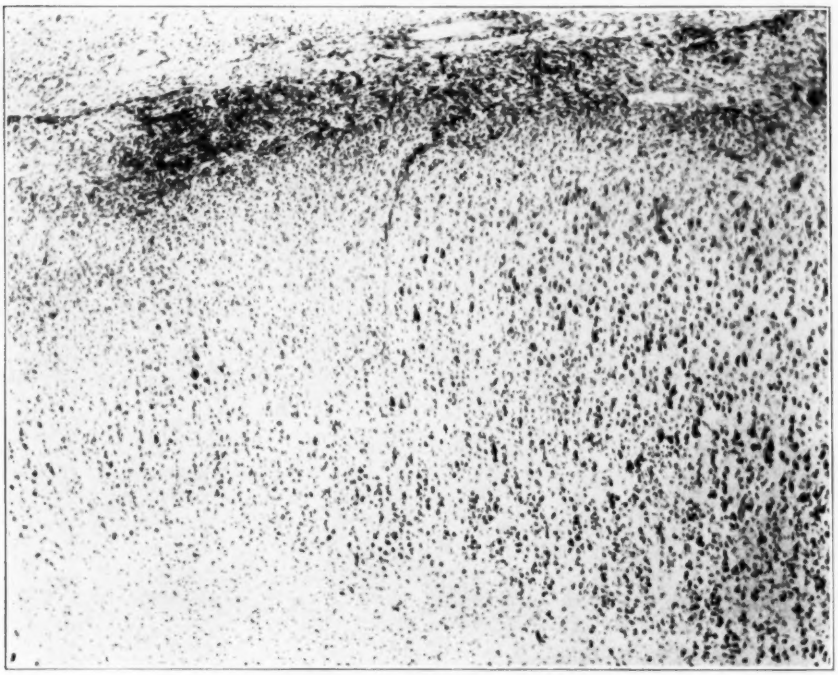


Fig. 3.—A photomicrograph showing destruction of the superficial layers of the motor cortex of a monkey by the application of heat at 50 C. for thirty seconds. The survival time was twelve days. The dura is adherent to the cortex, which is not the case after a survival time of seven days. Nissl stain; magnification, × 50.

quite suitable for the purpose of laminar thermocoagulation, because the depth of the lesion at these low temperatures is somewhat irregular.

We now turn to the description of the changes found in the cortex in the chronic stages after thermocoagulation at the higher temperatures regularly employed.

It was found that four months after local thermocoagulation of the whole thickness of the cortex (at 80 C. for five seconds) the entire

devastated area as it appears after a survival time of seven days (fig. 1) has vanished. This means that not only the nerve cells are gone, which, as we said before, is already the case within thirty-six hours, but also that the glia cells and the other interstitial tissue have disappeared.

The disappearance of the glia in the "chronic" preparations indicates that the glia cells which take the Nissl stain in the preparations made after a survival time of seven days must have been killed too and that they appear only as "skeletons." There is, therefore, a marked difference between the behavior of the nerve cells and that of the glia with respect

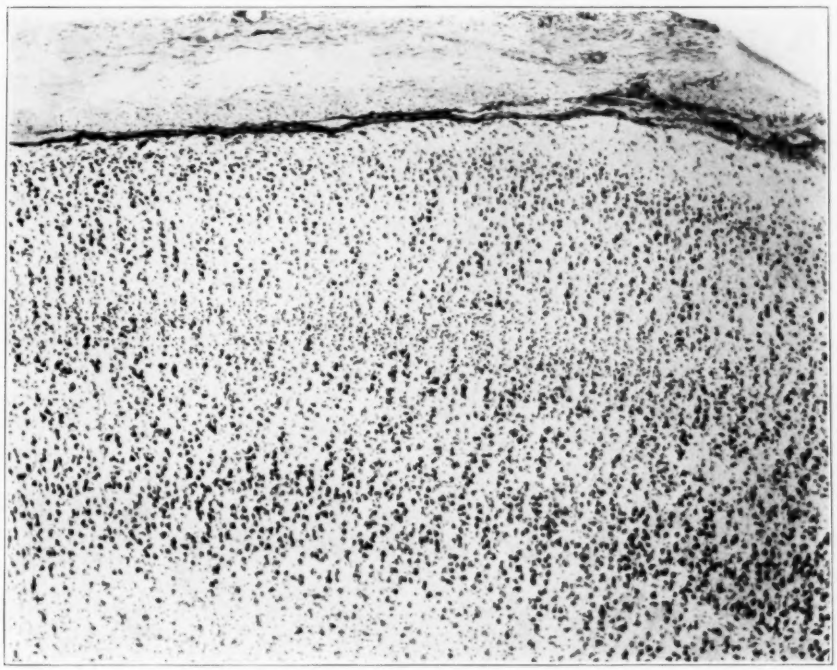


Fig. 4.—A photomicrograph showing the normal appearance of the motor cortex of a monkey after the application of the unheated apparatus for sixty seconds. Figures 3 and 4 show preparations from immediately adjacent areas in the same monkey. This section demonstrates that the pressure of the heating apparatus on the cortex, even when applied for as long as one minute, does not produce any injury. The survival period was twelve days. The dura is adherent to the cortex as in the preparation shown in figure 3. Nissl stain; magnification, × 50.

to heat: The first group of cells disappears completely within thirty-six hours, whereas the glia is present and stainable seven days, and even twelve days, after thermocoagulation. Therefore the initial conception of one of us (D. de B.) that these glia cells survive is wrong, as is

shown by the fact that they also finally disappear; the most plausible assumption now is that they are killed simultaneously with the nerve cells.

In the monkey to which figures 5, 6 and 7 have reference, the whole thickness of the cortex on the convexity of the precentral and postcentral sensorimotor arm area was destroyed by thermocoagulation (80 C. for five seconds). Figures 5, 6 and 7 illustrate a part of the lesion after a survival period of four months. In the center is the sulcus centralis; on one side are the remnants of the precentral, on

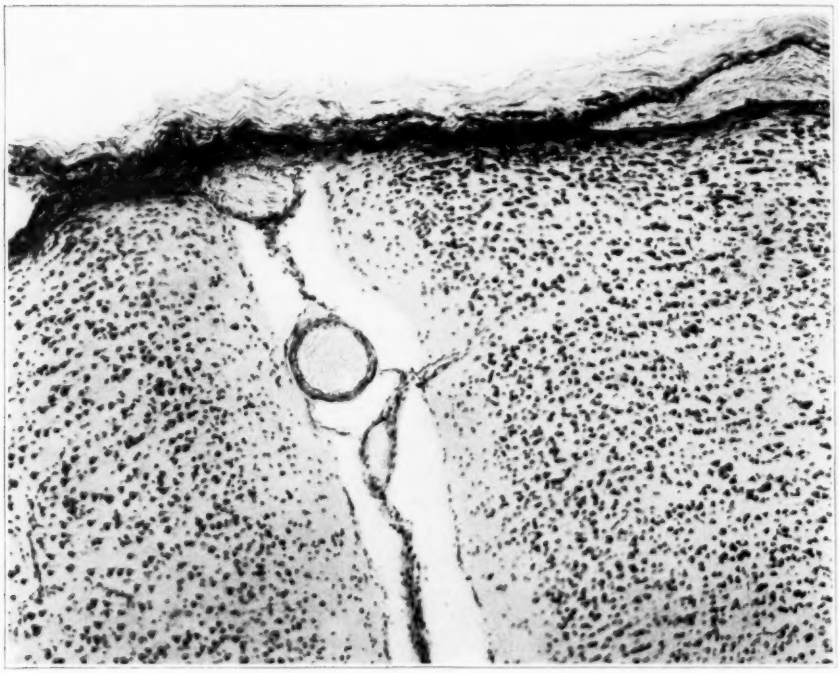


Fig. 5.—A photomicrograph of the precentral and postcentral gyri of a monkey in which the whole sensorimotor arm area on the surface of the hemisphere was destroyed by thermocoagulation at 80 C. for five seconds. The survival period was four months. Note (1) the absence of the destroyed cortex on the crests of the gyri, (2) the normal appearance of the remaining cortex, and (3) the new position of the meninges. Nissl stain; magnification, × 75.

the other, those of the postcentral, cortex. These parts of the cortex were not reached by the applied heat. The thickened dura lies immediately over the apparently normal cortex. Figure 7 represents diagrammatically what has happened. The cortical area outlined with dotted lines was heated. After four months the dura rests at its new level on the remaining cortex on each side of the large sulcus (sulcus centralis).

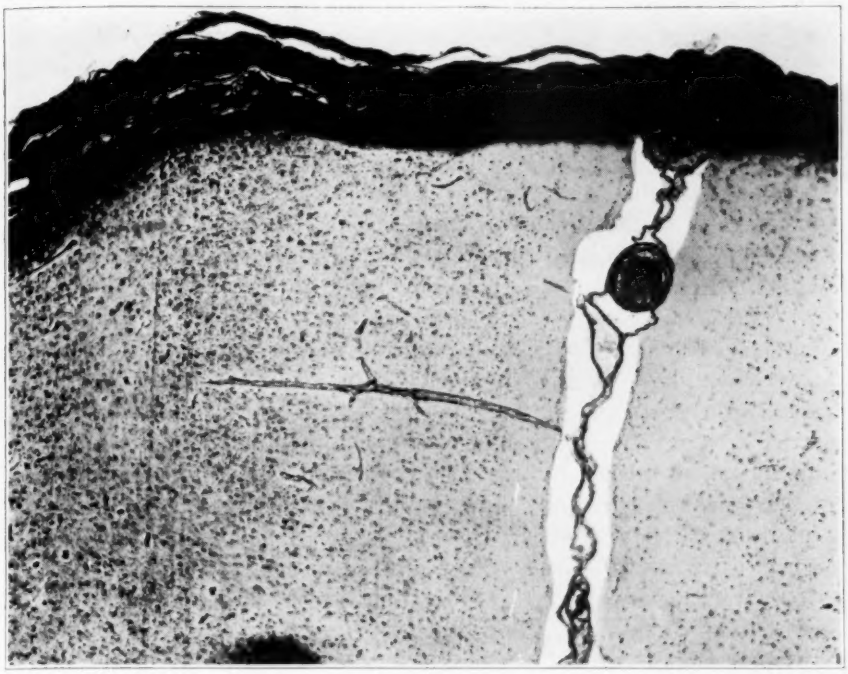


Fig. 6.—A photomicrograph of the area shown in figure 5 prepared by the Klarfeld method. Note the absence of proliferation of the connective tissue, i. e., the lack of scar formation; magnification, × 57.

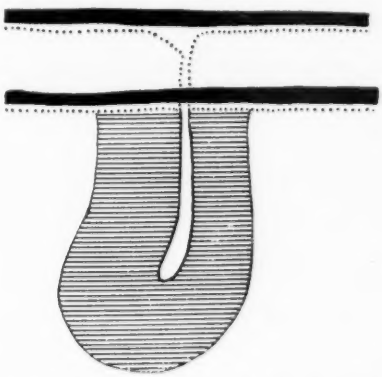


Fig. 7.—A diagrammatic representation of the part of the cortex shown in figures 5 and 6. The drawing shows (1) the extent of the devastated area as it would appear in the "acute" and the "subacute" preparation, which has disappeared in the "chronic" preparation, and (2) the new position of the meninges after the disappearance of the killed portions of the cortex. The solid portion indicates the dura, and the dotted lines the outline of the cortex which has disappeared.

We wish to emphasize the fact that the remaining cortex shows hardly any alteration and that the nerve cells now lying immediately below the dura are normal, as is also the general arrangement of the nerve cells. No sign of scar formation (retraction and fibroblastic proliferation) can be seen. This is especially clear in the sections prepared by the Klarfeld method (fig. 6).

We think that it can be safely said that such a final result is not met with in cortical lesions produced by any present-day neurosurgical method. Furthermore, it can be stated that signs of postoperative irritation have never been observed in the many animals we have employed.

The microscopic observations on the "chronic" preparations, together with the absence of postoperative irritation, strongly suggest that this method of thermocoagulation at 80 C. may be of value in neurosurgery. The fact that the lesions produced by this method are strictly localized to the heated area and that in the course of a few months all the elements within the heated area have disappeared without any noticeable damage to the immediately adjacent cortex makes us believe that this method can be used advantageously in special cases in which a sharply restricted extirpation of some parts of the convexity of the cortex is necessary. We have in mind especially cases of motor or sensory cortical epilepsy which are due to more or less localized, irritative alterations of the motor or sensory cortex. We fully realize that this method, at least in its present form, is applicable only to the cortex so far as it lies on the surface of the hemisphere. On the other hand, we think that, even restricted to that territory, the method offers so many advantages that we are justified in giving this paper the subtitle: "A Suggestion to Neurosurgery."

SUMMARY

The changes in the cerebral cortex produced by thermocoagulation through local application of heat at from 50 to 80 C. for short periods of time are described. The most suitable temperatures for laminar thermocoagulation of the cortex are from 65 to 80 C.

The depth of the lesion depends on the temperature applied and the duration of the application.

Following thermocoagulation at a temperature between 65 and 80 C. all the nerve cells have disappeared in the heated area after thirty-six hours. After from seven to twelve days the heated area appears as a devastated region, sharply delimited from the normal surrounding cortex by a wall of proliferated glia and fibroblasts. Inside the heated area the glia cells are still present and staining after twelve days.

Application of lower, though still supernormal, temperatures to the cortex results in typical changes. Even the application of 50 C. for half a minute to the cortex results in the death of all the nerve cells in the heated area; they have disappeared after thirty-six hours.

It is of interest that in the "chronic" preparations (survival period of four months) *the whole devastated area has disappeared.* Not only the nerve cells, but also the neuroglia, the blood vessels, the interstitial tissue and the wall of proliferated glia and fibroblasts, have disappeared. This fact proves that the glia present and staining in the "acute" preparations is no longer alive but has also been killed by the thermocoagulation.

Scar formation and retraction of the adjacent cortex are absent in "chronic" preparations. This observation suggests the usefulness of this method in neurosurgical procedures on man.

Clinical Notes

MENINGO-ENCEPHALITIS CAUSED BY CYSTICERCUS CELLULOSAE

VERA B. DOLGOPOL, M.D., AND MARCUS NEUSTAEDTER, M.D., PH.D.
NEW YORK

Cysticerci, the larvae of several intestinal tapeworms, are frequently encountered in internal organs, chiefly in the muscles, of various domestic and wild animals. In man the most frequent sites are the eye, the brain and the skin. The cysticercus affecting the eye and other organs of man is usually Cysticercus cellulosae, the larva of Taenia solium, the porcine tapeworm, but several cases of infection with Cysticercus bovis, the larva of Taenia saginata, the bovine tapeworm, are known (von Herrenschwand [1] and Fontan [2]). The cysticercus found in the brain is apparently always Cysticercus cellulosae.

Although second in frequency (Vosgien [3]), cysticercosis of the brain is the most important form of infestation because of the gravity of the prognosis. Clinical diagnosis is difficult because of the lack of a characteristic clinical picture and because of the variability of the seat of the lesion and its frequently disseminated character. Diagnosis is therefore most often made with the aid of a necropsy.

REPORT OF A CASE

History.—L. A., a married Mexican woman, aged 30, a dressmaker, who had been in the United States for six years, was admitted to the Central Neurological Hospital on May 13, 1932. The family history contained no facts bearing on the present illness, and in the personal history the only relevant fact was a miscarriage, following a fall, one month before, and another five months after, the onset of the illness. One child was living and well. The present illness had begun one year before admission to the hospital with constant headache, radiating from the frontal to the occipital region; the headache was worse toward evening. Five months later vision in the left eye became blurred, and the patient complained of seeing red and blue lights. A few weeks later she began to vomit, usually in the morning before breakfast (the vomiting was described as projectile), and convulsive seizures of the left arm and leg occurred. Later these symptoms subsided and, while the vision in the left eye began to improve, vision in the right eye became blurred. One month before entering the hospital, the patient was at the New York Eye and Ear Infirmary; vision in the right eye was found to be 20/70; vision in the left eye, 20/50. Lumbar puncture showed the pressure of the

From the Pathologic Laboratories and the Neurological Division of the Central Neurological Hospital.

1. von Herrenschwand, F.: Zwei Fälle von subretinalem Zystizercus, Wien. klin. Wchnschr. **29**:1132, 1916.

2. Fontan, C.: Cysticercus bovis chez l'homme, Gaz. d. hôp. **92**:183, 1919.

3. Vosgien, Y.: Le cysticercus cellulosae chez l'homme et chez les animaux, Thèses de Paris, no. 373, 1911.

cerebrospinal fluid to be 440 mm. of water; the fluid gave a meningitic colloidal gold curve and contained 100 white cells per cubic millimeter, 13 per cent of which were eosinophils; no parasites or ova were found in the feces. From the infirmary the patient was transferred to the Central Neurological Hospital.

Examination (by Dr. Neustaedter).—The pupils were equal and regular in outline; they hardly reacted to light, but reacted promptly in accommodation and in convergence. The right disk was oval and normal; the left showed papilledema of 4 diopters. The visual fields were normal for all colors, with dyschromatopsia. There were a slight left exophthalmos and edema of both lids, but without pulsation of the eyes. Scleral reflexes were absent; corneal reflexes were present. The reflexes of the upper extremities were brisk and equal on the two sides; there was no Hoffmann sign. The abdominal reflexes were absent on both sides. Suprapatellar reflexes could not be elicited. The patellar reflexes were brisk on both sides; there was no patellar clonus. There was a right associated, but no true, Babinski sign. No other pathologic reflexes were found. The ocular muscles were not impaired. The tongue protruded in the midline. Motor power was not impaired. There was no ataxia. A slight intention tremor was present in both hands. With the exception of the left optic nerve all the other cranial nerves were intact.

The pressure of the cerebrospinal fluid was 22 mm. of mercury; there was no block. The fluid was clear and contained 14 cells per cubic millimeter with 75 per cent lymphocytes; globulin was increased; the fluid contained 84 mg. of dextrose and 133 mg. of protein per hundred cubic centimeters; the colloidal gold reaction was 0122333210.

Diagnosis.—Despite negative Wassermann and Kahn reactions of the blood and a negative Wassermann reaction of the spinal fluid, the case was believed to be one of some retrobulbar lesion, probably a gumma.

Course.—Encephalography on May 20, with the withdrawal of 140 cc. of fluid and the injection of 140 cc of air, showed normal lateral ventricles and dilatation of the isthmus, which was interpreted as a possible site of moderate obstruction.

Because of eosinophilia in the blood (10 per cent), detailed cytologic examination of the cerebrospinal fluid was made and revealed: 12 cells per cubic millimeter, 26 per cent eosinophils, 24 per cent neutrophils and 50 per cent lymphocytes. These observations led us to suspect a parasitic infection of the meninges or brain. A search was made for hooklets in the cerebrospinal fluid and for ova in the feces, but without success.

In view of the negative results, the diagnosis of retrobulbar gumma, with gummatous meningitis, was maintained and antisyphilitic treatment was given. The patient received twelve injections of silver arsphenamine, twelve of a suspension of bismuth salicylate in oil in six months and large doses of potassium iodide.

Two months after admission vision in the right eye was 10/200, and in the left eye, 20/50. In September 1932, no eosinophils were found in the cerebrospinal fluid or in the blood. In October, there developed jacksonian attacks, which were limited to the right side and preceded by paresthesia of the right upper and lower extremities. The neurologic condition was unchanged, except for slight right hemiparesis and hemihypesthesia. Two weeks later the visual fields were constricted, more in the left eye, and there was a central scotoma on both sides. On December 7, the patient had a general clonic convulsion, with loss of consciousness, which lasted for about three minutes; there was no bleeding or frothing

from the mouth. Following this attack vision began to fail more rapidly. On December 27 there was amblyopia; vision was limited to counting fingers; there were complete primary optic atrophy on the right and marked papilledema on the left; the pupillary reflexes were not tested because a mydriatic had been administered; the ocular movements were intact; there was no nystagmus; the corneal reflexes were present; the pharyngeal reflex was absent. The senses of smell and taste were intact; all cutaneous tendon reflexes were present and were slightly more active on the right; the abdominal reflexes were diminished; there was no patellar or ankle clonus; there was plantar flexion on the left, with slight fanning of the toes and a tendency to extension of the great toe on the right, and a right Oppenheim reflex; there was a slight weakness of the extensors of the right foot; the finger-to-nose test was well executed; the heel-to-knee test showed slight dysmetria; gait was steady, without ataxia or spasticity; sensibility was not disturbed; there was considerable tenderness on percussion over the left temporal bone; the Rinne test was more intense on the right than on the left; the patient complained of noises in the left ear; there was also complaint of an intermittent headache in the left side of the head. Because the patient was threatened with blindness right subtemporal decompression was decided on.

Because of the scattered and indefinite symptoms and of the repeatedly negative Wassermann reaction of the blood and spinal fluid, a tentative preoperative diagnosis of sarcomatosis of the base of the brain was made.

Operation.—On December 28, under 2 per cent procaine hydrochloride anesthesia, an opening, 1 inch (2.5 cm.) wide, was made in the right temporal region of the skull. The dura and brain were under pressure and bulged through the opening. A small tumor mass was seen on the under surface of the dura and was removed, with its dural attachment, the opening having been enlarged for this purpose. The wound was sutured in layers.

Biopsy.—The nodule was round and firm, 1.5 cm. in diameter, and had a small piece of dura attached. The specimen appeared grossly to consist of whorls of fibrous tissue. Microscopically, there were whorls of fibers, only some of which stained red with the van Gieson stain, and a large number of oval and elongated pale nuclei. In places a few small arteries with calcified intima formed the center of the whorls. The anatomic diagnosis was meningioma.

Postoperative Course.—On the day after operation there was paralysis of the left side of the body, including the face. A Babinski reflex was present on the left. The paralysis of the leg subsided a day later, but the paralysis of the arm and face remained unchanged. On Jan. 3, 1933, the patient was completely amaurotic, with primary optic atrophy on the right and complete secondary atrophy on the left. There was no essential change until January 18, when a small purulent discharge appeared from the wound. Chills developed, the temperature not rising over 103 F. The lower end of the wound was opened, and a small pus pocket was drained. The patient died on Feb. 7, 1933.

The total duration of the disease was one year and nine months.

Necropsy.—Gross Observations: Necropsy was performed two hours after death. The body weighed about 110 pounds (49.9 Kg.). Rigor mortis was absent. A partly healed operative wound, 9 by 4 cm., was present in the right temporal region, extending below the hair-line. The lower end of the wound was open, and pus was oozing from it. Cultures from the pus yielded Staphylococcus aureus. The skin was adherent to the dura in the region of the surgical field. The meninges did not bulge. The skull was thin and presented a number of thin, slightly elevated ridges on the inner surface. The brain was slightly edematous.

A large area of softening was present in part of the right parietal lobe, part of the temporal lobe and the lower part of the motor and sensory regions. The pia-arachnoid of the upper and lateral surfaces of the brain was smooth. On the lower surface a heavy plastic exudate was present over the peduncles, the pons and the medulla, extending apparently to the spinal cord. A structure resembling a tassel of vesicles was seen emerging from the right sylvian fissure; this structure was easily displaced, being slightly attached only to the meninges in the fissure. Other groups of more sharply defined vesicles were seen on either side of the pons; the pedicles of these vesicles were submerged in the sulci along the blood vessels, not penetrating, however, into the brain substance. Two tassel-like groups of vesicles were present on either side of the pons and met over the quadrigeminal bodies (fig. 1). The fourth ventricle and the aqueduct of Sylvius

Fig. 1.—Cortical anemic infarct in the right hemisphere. Chains of vesicles on either side of the pons are cut through. The arrows point out unsectioned vesicles.

were filled with a dry, cheesy material. A grayish filmlike exudate covered the surface of the lateral ventricles, being thicker in the right. No vesicles were found in the ventricles, choroid plexuses or brain substance. The orbits were not opened. Smears from the plastic exudate were negative for Bacillus tuberculosis; no other bacteria were found in the smears. A few colonies of Staph. aureus were grown from the exudate (the possibility of contamination in removing the brain, however, could not be excluded). The chain of vesicles from the sylvian fissure (fig. 2) was sectioned along the stem, and presented a twisted tubular structure with evaginations; no parasite body was found in this structure. The diagnosis was: infestation with Cysticercus racemosus.

Viscera: Other organs showed no gross pathologic changes (microscopically, there were minute deposits of amyloid in some malpighian bodies of the spleen). No vesicles were present in the skin, abdominal muscles or internal organs. No tapeworm was found in the intestinal contents.

Microscopic Observations: The cysts: In mounted preparations of a piece of the entire cyst wall the outer surface presented uniform, evenly distributed, blunt papillary elevations. In sections from the cyst wall embedded in paraffin, the papillary elevations were seen to be formed by a dentate membrane (cuticular layer) which appeared as a refractile structure resembling an elastica (fig. 3). In staining properties, however, the cuticular layer differed from elastic tissue: It stained purple with hematoxylin-eosin and reddish with the Weigert elastica stain; with cresyl violet it stained violet, while the elastica of the arteries remained unstained. In places short hairlike structures were seen on the outer surface of the cuticle. The rest of the cyst wall consisted of a meshwork of thin, refractile fibers forming a plexus-like arrangement at the inner surface. Several rows of pale round nuclei were present in the outer part of the mesh, beneath the cuticle.

Fig. 2.—Chain of vesicles from the right sylvian fissure (slightly smaller than natural size).

In some places the mesh above the nuclei contained droplets which tended to become confluent into large oval bodies occupying the entire thickness of the wall or to break through into the lumen of the cyst. The droplets and the oval bodies stained pink with eosin, and gave the red reaction of hyalin with the picrofuchsin stain. In some cysts the nuclear layer was absent, and oval, blue-staining calcific bodies, larger than the nuclei, were scattered throughout the thickness of the cyst wall. The total thickness of the cyst wall was from 80 to 200 microns. Some cysts were empty except for thin septums running through them. Other cysts contained a pink-staining hyaline substance similar to the hyaline bodies of the cyst wall. Where the cyst wall was disintegrated the hyaline material adjoined the reactive capsule, which is a structure belonging to the host, or else cells from the surrounding exudate penetrated into the interior of the cyst.

A structure resembling a dead body of a parasite was found in one cyst situated between the convolutions of the vermis (fig. 4). It consisted of several rings which stained dark blue with hematoxylin and eosin and contained a coagulated, fibrillar material. Some rings showed the presence of cellular elements, while

others appeared almost homogeneous and showed the staining characteristics of the cuticle. No hooklets were seen. Another cyst, in one of the tassels bordering on the pons, contained a similar structure.

The reactive capsule: A capsule of an early reactive type was present around two small cysts. Nearest to the cysts was a layer of lymphocytes, which was identical with the exudate covering the adjacent structures; outside the lymphocytes were a layer of epithelioid cells and a few giant cells with nuclei resembling those of the epithelioid cells. In other places the reactive capsule consisted of two or possibly three layers (fig. 5). Nearest to the cyst (or to its escaped hyaline

Fig. 3.—Wall of the cysticercus cyst consisting of the cuticular, the germinative and the parenchymatous layers, with hyaline bodies in the latter. Hematoxylin and eosin; Leitz periplane eye-piece 25, objective 3.

contents where the wall was disintegrated) was a layer of multinucleated giant cells of the foreign body giant cell type (or occasionally resembling the Langhans' giant cells), with occasional epithelioid cells between them. The second layer consisted of thick collagenous fibers, with occasional plasma cells and lymphocytes. Outside this layer was a rather thick layer of granulation tissue consisting of lymphocytes, plasma cells and occasional congested capillaries; these structures could belong to the capsule or to the meninges. In some places the inner layer of the capsule presented a caseous appearance and contained blue clumps of calcium deposits.

The plastic exudate: The exudate covering the base of the brain consisted of meshes of fibrin with a large number of cellular elements, most of which were lymphocytes. On the surface some polymorphonuclear neutrophils were present between the lymphocytes, while in the deeper layers there was a heavy admixture of plasma cells. Close to the nerve tissue a large number of round phagocytes, with refractile granules in the cytoplasm, and some giant cells with many centrally located round nuclei were seen. The round phagocytes were especially numerous in the proximity of blood vessels. The presence of epithelioid cells in

Fig. 4.—Annular structures in a cyst which were interpreted as the degenerated body of a parasite. Hematoxylin and eosin; Leitz periplane eye-piece 16, objective 3.

the deep layer of the exudate indicated the proximity of a parasitic cyst. No eosinophils were found in any part of the exudate.

The blood vessels: The arteries at the base of the brain and near the large area of softening showed the typical cysticercus endarteritis. The degree of endarteritis varied from eccentric or warty excrescences of the intima to a circular thickening and bridging of the intima, causing an almost complete occlusion of the lumen (fig. 6). The endothelial cells showed some accumulation only over the localized thickenings. Beneath the endothelial cells the intima contained a large number of elongated or stellate young connective tissue cells, radiating to

the lumen in local intimal thickenings, and parallel to the lumen in more advanced endarteritis. The elastica remained in its normal position and did not split; small areas of resorption of the elastica were seen in a few larger arteries (fig. 6). The muscularis was usually intact, but a slight fibrosis was seen in several arteries. The adventitia often showed an extensive infiltration with plasma cells and lymphocytes, which was at times continuous with the surrounding exudate. The occurrence of granular phagocytes near arteries has already been mentioned. The basilar artery showed some lymphocytic collections in the intima.

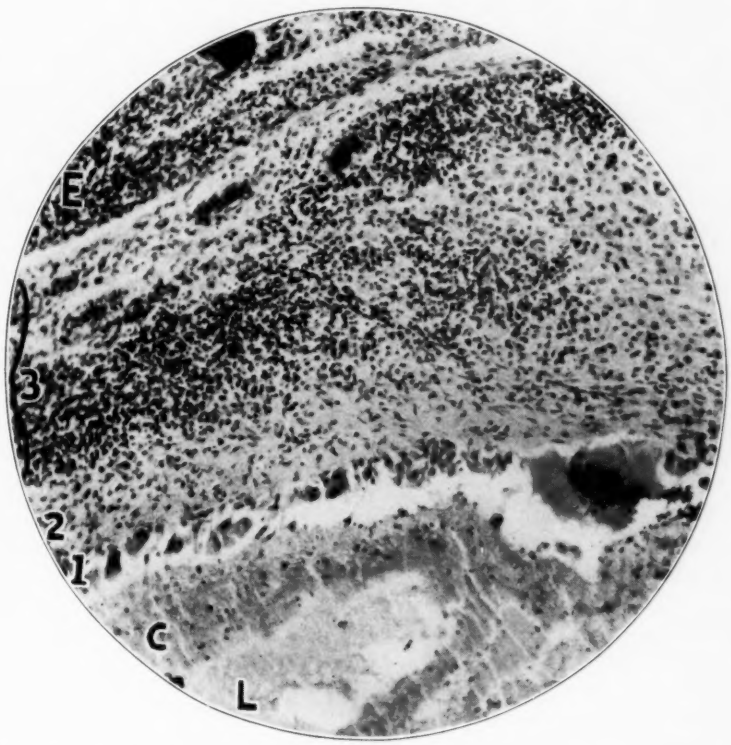


Fig. 5.—A fully developed reactive capsule: *L*, lumen of the parasitic cyst; *C*, degenerated cyst wall; *1*, layer of giant and epithelioid cells; *2*, collagenous fibrous layer; *3*, granulation tissue; *E*, meningeal exudate. Hematoxylin and eosin; Leitz periplane eye-piece 25, objective 3.

Another kind of arterial change was observed in arteries embedded in the areas of the exudate abounding in polymorphonuclear cells. It consisted of an acute thrombosis, with accumulation of polymorphonuclear leukocytes in the lumen, and with a diffuse degeneration of the arterial wall which appeared to be penetrated with fibrin. These arterial changes are not characteristic of cysticercosis and could be explained by a coexisting pyogenic infection arising from the cutaneous wound.

The veins at the base of the brain showed some swelling of the endothelial layer but no other intimal changes. A small number of plasma cells were seen in the adventitia of some veins.

The brain tissue: The tissue at the base of the brain and along the ventricular surfaces showed a number of small, thick-walled arteries, with a large number of plasma cells and lymphocytes in the adventitial spaces (fig. 7). The infiltration with these cells extended also into the brain tissue. The ependyma of the ventricles and of the aqueduct showed warty elevations of the ependymitis granulosa. The choroid plexuses were edematous and contained fibrin and numerous plasma

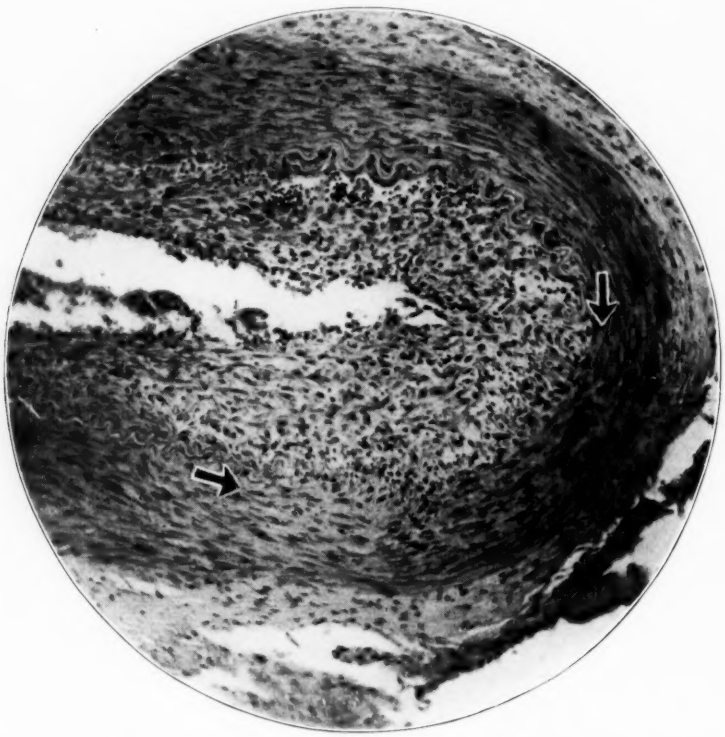


Fig. 6.—Arteritis of the basilar artery. The elastica resorbed between the arrows. Hematoxylin and eosin; Leitz periplane eye-piece 25, objective 3.

cells in the stroma. The free exudate filling the fourth ventricle and the aqueduct and extending into the lateral ventricles consisted of fibrin, necrotic round cells, lymphocytes and a small number of polymorphonuclear cells. The large softening in the right hemisphere presented a cortical infarction, with disappearance of nerve cells. Some areas showed necrotic brain tissue, with minute hemorrhages and collections of granular phagocytes, while others showed an advanced organization, with a large number of small blood vessels and numerous astrocytes. A small area of softening on the ventral aspect of the left temporal lobe showed minute hemorrhages and small arteries occluded with lymphocytic plugs. Astrocytes were present in the necrotic tissue, and granular phagocytes were present at the periphery.

In parts remote from the areas of softening and from the immediate neighborhood of the base of the brain or of the ventricular surfaces, no vascular changes were seen and the nerve cells were intact (cresyl violet stain). The number of glia cells was not excessive, except in the areas of softening and around perivascular infiltrates near the ventricular surface. The microglia showed no rodlike arrangement and contained no iron granules. The methods used for the study of the glial elements were the Globus modifications of the Cajal and Hortega methods and the prussian blue reaction for iron.

The optic nerves and the chiasm were covered with an exudate consisting of lymphocytes and a large number of cells with pale oval nuclei, apparently adventitial cells. Small groups of plasma cells were present around small blood vessels within the nerves. A few astrocytes were present in the right optic nerve.

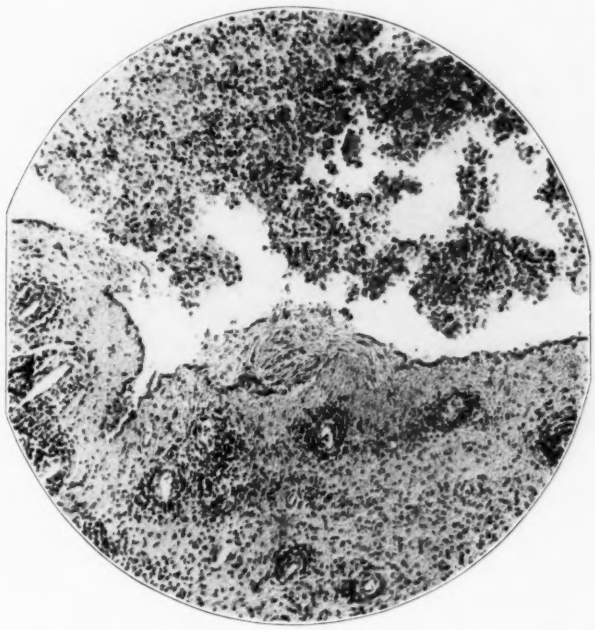


Fig. 7.—Section of floor of the fourth ventricle with perivascular infiltration, ependymitis granulosa and exudate in the fourth ventricle. Hematoxylin and eosin; Leitz eye-piece 10, objective 3.

The pia over the medulla was thickened and contained plasma cells, lymphocytes, adventitial cells and melanophorous cells. Plasma cells and lymphocytes surrounded the roots of nerves.

Summary of Pathologic Changes.—There were: (1) meningo-encephalitis and choroiditis caused by Cysticercus racemosus; ependymitis granulosa; (2) cysticercus endarteritis at the base of the brain and in the branches of the right middle cerebral artery, distal to the lenticulostriate artery, and (3) cortical infarction.

A chain of cysts was sent for identification of the parasite to the National Institute of Health in Washington, D. C. The report of Mrs. Mabelle O. Nolan,

zoologist of the Institute, was: "The cysticercus is the racemose variety of Cysticercus cellulosae, the larval form of the pork tapeworm, Taenia solium."

COMMENT

Mode of Infection.—Infection with cysticerci occurs through ingestion of ova of a tapeworm. Hosts of an intestinal tapeworm may become infected by introducing ova with the food while eating with soiled hands or by regurgitation of mature segments into the stomach during vomiting. Such cases, however, are not frequent; of 579 patients with cysticercosis investigated by Vosgien, 62 had an intestinal tapeworm. In the majority of cases the infection is introduced from outside. In rare cases helminthiasis was found in a member of the family of a patient with cysticercosis. The usual mode of infection is through consumption of uncooked vegetables which have been soiled with human excreta or with fertilized soil containing ova of parasites (Henneberg,[4] Heilmann[5]). In the stomach the ingested ovum liberates the embryo, which works its way into the circulation and through some artery is carried to the eye, the brain or other organs. Experimentally, in animals, adult cysticerci develop in about ten weeks after ingestion of the ova. The cysticerci may live for many years (thirty-three years in the case of Stoess[6]). Dead cysticerci may become calcified.

Incidence of Cysticercosis in Man.—The incidence of cysticercosis varies with the locality, being more frequent in regions in which there is a greater consumption of pork and in which the inspection of meat is less thorough (Vosgien). The incidence has varied considerably in different periods, showing a decided decrease since the introduction of meat inspection, which has led to a diminution of intestinal infestation with tapeworms (2 per cent of the necropsy material showed such an infestation in 1866; the figure was 0.18 per cent from 1896 to 1902 [Virchow[7]]). During the World War helminthiasis increased as a result of temporary laxity in the inspection of meat, the lack of facilities for cleanliness contributing measurably to the increase of cysticercosis among persons connected with war activities (Uhthoff,[8] von Herrenschwand[1] and Antonow[9]).

Few reports of human cysticercosis were found in North American literature. Turnbull[10] reported a case of an ocular parasite and mentioned 3 other cases presented by other authors at medical meetings. Foster and Gately[11] reported

4. Henneberg, R.: Die tierischen Parasiten des Zentralnervensystems: Der Cysticercus cellulosae, in Lewandowsky, M. H.: Handbuch der Neurologie, Berlin, Julius Springer, 1905, vol. 3, p. 643; Die Parasiten des Centralnervensystems, in Kraus, F., and Brugsch, T.: Spezielle Pathologie und Therapie, Berlin, Urban & Schwarzenberg, 1919-1925, vol. 10, pt. 2, p. 165.

5. Heilmann, P.: Beitrag zur Pathologie der Hirncysticercose, Virchows Arch. f. path. Anat. **286**:176, 1932.

6. Stoess, L.: Ein Fall von Cysticercus racemosus des Gehirns, Erlangen thesis, 1901.

7. Virchow, R., quoted by Vosgien.[3]

8. Uhthoff, C. A.: Vier Fälle von Cysticercus subretinalis bei Kriegsteilnehmenden, Klin. Monatsbl. f. Augenh. **64**:180, 1920.

9. Antonow, A.: Ueber die Art der Kapselbildung bei Hirncysticercose, Virchows Arch. f. path. Anat. **285**:485, 1932.

10. Turnbull, C. S.: On Cysticercus cellulosae, Tr. M. Soc. Pennsylvania **12**: 674, 1879.

11. Foster, L. A., and Gately, T. T.: Encysted Muscular Parasites, South. M. J. **21**:190, 1928.

a case of cysticercosis of the muscles. Luney [12] described a case of cysticercosis of the meninges (four separate cysts with parasites in them).[13]

Incidence and Distribution of Cysticerci in the Brain.—From necropsy material, the frequency of cysticerci in the brain varies from 1 in 7,000 (Bollinger [14]) to 1 in 830 cases (Heilmann, Zwickau, 1932) and to 1 in 146.5 cases (Jacoby [15]). Cysticercosis of the brain appears to be especially prevalent in Russia; Winogradowa [16] observed 12 cases in two and one-half years. Calcified cysticerci may be found accidentally at autopsy.

Cysticerci may be single or multiple in the brain. In multiple cysticercosis the number of parasites is usually not great, but at times they may be present in hundreds (Lazarew [17]). The cysts may develop in a ventricle (usually the fourth), in any part of the cortex, in the substance of the brain, in the meninges of the convexities or at the base of the brain. In the latter cases the cysticercus often assumes a racemose (grapelike) appearance. The racemose cysticercus may show a great number of vesicles, which are considered to be evaginations of the cyst of a single parasite or perhaps of a small number of independent parasites. The vesicles may become altogether separated from the original cyst and continue an acephalic existence, so that the head of the Cysticercus racemosus is rarely found (Zenker [18] and Vosgien). The racemose variety is seen in about one sixth of the cases of cysticercosis of the brain (50 of 330 cases of Vosgien; 1 of 6 cases of Heilmann; Opalski's [19] incidence of racemose cysticerci is somewhat higher, 4 of 12 cases). Together with a racemose cysticercus of the basal meninges, independent ordinary cysticerci may occur in the brain and in the ventricles.

Diagnosis of Cysticercosis of the Brain.—1. Clinical: No single clinical picture can be expected. The varying tension of the vesicular contents, especially in the racemose forms, the reactive changes in the meninges and vascular changes contribute to the diversity and variability of the clinical manifestations. These are usually: headaches, temporary or permanent paralyses, epileptiform seizures, vomiting, vertigo, mental disturbances and a number of other symptoms and signs that occur in various organic diseases of the brain and meninges. Some or all of the manifestations may subside temporarily. Hydrocephalus may be observed if the outflow of the cerebrospinal fluid is obstructed by ventricular cysts or

12. Luney, F. W.: Cysticercus of Taenia Solium in Human Brain, Canad. M. A. J. **14**:143, 1924.

13. In the case of Strauss and Globus (Invasion of the Brain by Parasitic Cysticercus, abstr., Arch. Neurol. & Psychiat. **25**:210 [Jan.] 1931) the parasitic nature of the lesions could not be established with certainty on further examination (personal communication to one of us).

14. Bollinger, O.: Ueber Cysticercus cellulosae im Gehirn des Menschen, München. med. Wchnschr. **35**:516, 1888.

15. Jacoby, E.: Zwei Fälle von Cysticercus cerebri mit Stauungspapille, Klin. Monatsbl. f. Augenh. **41**:223, 1903.

16. Winogradowa, quoted by Antonow.[9]

17. Lazarew, W.: Zur pathologischen Anatomie der Cysticercose des Gehirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:667, 1926.

18. Zenker, F. A.: Ueber den Cysticercus racemosus des Gehirns, Beitr. z. Anat. u. Embryol. als Festg. f. Jacob Henle, 1882, p. 119.

19. Opalski, A.: Histopathologische Veränderungen des zentralen Nervensystems bei Zystizercose, und ihre Pathogenese, Bull. internat. Acad. polon. d. sc. et d. lett. Cl. méd., Oct.-Dec., 1931, p. 276.

exudate. Bruns' sign (vertigo on rapid displacement of the head) is considered characteristic in cysticercus of the fourth ventricle. However, usually one cannot make a definite diagnosis, beyond establishing the presence of an organic disease of the brain and meninges. The presence of cutaneous cysticerci occasionally helps in making a clinical diagnosis of cysticercosis of the brain (Busse [20]).

2. Laboratory: Examination of the feces for ova is usually of little help, as the tapeworm is not often found in the intestinal canal of patients with cysticercosis. The finding of ova is of diagnostic significance.

The cerebrospinal fluid is often abnormal. In many cases the fluid is under increased pressure (620 mm. of water in the case of Stern; [21] 440 mm. of water in our case). Globulin is often increased. The colloidal reactions may be of syphilitic or dementia paralytica type (Kulkov [22] and Rizzo [23]). In our case the colloidal gold curve was at first meningitic but later changed to a syphilitic type. An increased number of cells has been observed by several authors, the highest being 320 in a case of Guillain and his co-workers; [24] in our case there was a transient increase to 100 cells. The Wassermann reaction of the cerebrospinal fluid is usually negative; the amount of dextrose is within the normal range, and no tubercle bacilli are found.

An important diagnostic sign is eosinophilia of the blood and of the spinal fluid. Eosinophilia in the blood is encountered in a number of allergic somatic diseases, the existence of which must be excluded before its presence assumes significance. According to Henneberg [25] and Schilling [26] a mild eosinophilia may occur also in syphilitic meningitis, so that this condition must be considered in making a differential diagnosis, but a high percentage of eosinophils points to a parasitic disease and not to syphilis. Eosinophils in the spinal fluid in cysticercosis have been seen by Stern, Rizzo, Guillain and his co-workers, Schenk,[27] Beumer [28] and others. In several cases cysticercosis was diagnosed from eosinophilia of the blood, and especially from the presence of eosinophils in the spinal fluid. In our case a transient eosinophilia, both of the blood and of the spinal fluid, was observed, but its diagnostic significance was not fully appreciated; the possibility of a

20. Busse, W.: Beitrag zur klinischen Diagnostik der parasitären Erkrankungen des Zentralnervensystems, Arch. f. Psychiat. **95**:189, 1931.

21. Stern, A.: Ueber Cysticerken im IV Ventrikel, Ztschr. f. klin. Med. **61**: 64, 1907.

22. Kulkov, A. E.: The Diagnosis of Racemose Cysticercus During Life, Arch. Neurol. & Psychiat. **24**:135 (July) 1931.

23. Rizzo, C.: Diagnosi in vita di cisticercose cerebrale, Riv. di pat. nerv. **32**:952, 1928.

24. Guillain, G.: Péron, N., and Thévenard, A.: Le liquide céphalorachidien dans la cysticercose cérébrale, Compt. rend. Soc. de biol. **95**:455, 1926. Guillain, G.; Périsson, J.; Bertrand, I., and Schmite, P.: Cysticercose cérébrale racémeuse, Rev. neurol. **2**:433, 1927.

25. Henneberg, R.: Die tierischen Parasiten des Zentralnervensystems. Der Echinococcus, in Lewandowsky, M. H.: Handbuch der Neurologie, Berlin, Julius Springer, 1910, vol. 3, p. 693.

26. Schilling, V.: Das Blutbild und seine klinische Verwertung, Jena, Gustav Fischer, 1929, pp. 137, 218 and 325.

27. Schenk, P.: Ueber einen intra vitam diagnostizierten Fall von Cysticercus racemosus, Deutsche Ztschr. f. Nervenh. **66**:301, 1920.

28. Beumer, H.: Zystizerkenmeningitis, Deutsche med. Wchnschr. **56**:876, 1930.

parasitic disease was considered, but later the case was regarded and treated as syphilis. In many cases of cysticercosis no stained preparations of the sediment of spinal fluid were examined, so that probably many more cases of eosinophilia in the fluid were overlooked. The echinococcus, too, commonly produces eosinophilia, but the manifestations of this parasite in the brain point more to a focal expanding lesion, as in a tumor of the brain (Henneberg), while the symptomatology of cysticercosis of the brain, because of the dissemination of the lesions, is more suggestive of an inflammatory disease. Eosinophilia in parasitic diseases is a response to toxins eliminated by the parasites. The death of the parasite may reduce the number of eosinophils in the blood to normal figures, but it must be pointed out that an overwhelming infestation by parasites also may reduce the eosinophil counts. A complete disappearance of eosinophils from the blood is a sign of grave prognostic significance, whether in parasitic or in other diseases (Schilling). In our case the eosinophils disappeared completely from the spinal fluid and blood in the last five months of the patient's life; no eosinophils were found in the inflammatory exudate of the brain or in the reactive capsule. Immunologically, the disappearance of eosinophilia in a severe parasitic disease may be compared to the disappearance of reaction to tuberculin in moribund tuberculous patients.

In addition to the eosinophilia, the spinal fluid may show the presence of pieces of cyst wall; several instances of this condition have been reported (Stertz,[29] Morawiecka[30] and Hartmann[31]).

Serologic methods of diagnosis have been tried in cysticercosis, by analogy with the methods employed for the diagnosis of echinococcus disease. Since Meyer[32] found serologic group reactions between extracts of various types of Taenia and the blood of hosts of tapeworms, repeated attempts have been made to use echinococcus antigens for the diagnosis of cysticercosis. Positive reactions of complement fixation with echinococcus antigens helped to establish the clinical diagnosis of cysticerci in the brain in the patients of Busse and of Beumer. According to Weinberg[33] and Blumenthal,[34] the group reactions are produced only with the use of alcoholic extracts of echinococcus cysts of man or sheep as antigen, while the cyst fluid antigen is specific for the echinococcus and does not give the group reactions. The complement-fixation reactions are rarely accessible because of difficulty in securing the antigen. If positive, they are significant in the absence of intestinal parasites.

3. Pathologic: Diagnosis of cysticercosis of the brain is not always established at necropsy. Chains of meningeal cysticerci may be lost during the removal of the brain, so that a correct diagnosis may become next to impossible. In our case the cysts were collapsed and became visible only after the brain was submerged in the fixation fluid.

---

29. Stertz: Cerebrospinale Cysticerkose, Berl. klin. Wchnschr. **47**:461, 1910.

30. Morawiecka, quoted by Kulkov.[22]

31. Hartmann, F.: Cysticercosis cerebri diagnostiziert durch die Lumbalpunktion, Wien. klin. Wchnschr. **15**:547, 1902.

32. Meyer, K.: Zur Serodiagnostik der Echinokokkenerkrankung, Berl. klin. Wchnschr. **47**:1316, 1910.

33. Weinberg, M.: Séro-diagnostic de l'echinococcose, Ann. Inst. Pasteur **23**: 472, 1909.

34. Blumenthal, G.: Echinokokkenkrankheit, in von Kolle, W., and von Wassermann, A.: Handbuch der pathogenen Mikroorganismen, Jena, Gustav Fischer, 1912-1913, vol. 6, pt. 2, p. 1253.

If the body of the parasite is found the diagnosis is not difficult. In cases of acephalic parasites or when the parasite cannot be located diagnosis is made from the histologic structure of the cyst wall, as was done in our case. The cyst wall consists of three layers. According to Henneberg, the outer, wavy cuticular chitinous layer may show in places radial striation which accounts for a fuzzy appearance of the outer surface. The second layer contains a few rows of nuclei ("germinative layer" of Guillain). The third layer ("parenchymatous layer" of Guillain) consists of a network of refractile fibrils and may show calcium-containing bodies and, as in our case, droplets of a hyaline material.

The presence of a reactive capsule also helps in establishing the diagnosis of the parasitic nature of the lesions. In our case not every vesicle was surrounded by a capsule, some of them being merely embedded in the exudate covering the meninges. A layer of epithelioid cells, with occasional giant cells, outside a thin layer of exudate represented the early reactive capsule; in places the epithelioid layer was surrounded by a layer of collagenous connective tissue. The first layer of a fully developed capsule around degenerated cysts showed an almost solid layer of giant cells, with occasional epithelioid cells between them; the second layer consisted of thick collagenous fibers, with a few lymphocytes and connective tissue cells between them; the third layer, a granulation tissue with small blood vessels showing a perivascular infiltration with lymphocytes and plasma cells, merged gradually with the meninges.

The pathologic changes in the meninges, blood vessels and brain may bear a strong resemblance to syphilitic changes, thus adding to the difficulty of the pathologic diagnosis. Cysticercus meningitis resembles a gummatous lesion ("pseudogummatous meningitis" of Guillain). The arteries in the proximity of the cysts show changes which are not unlike Heubner's endarteritis. According to Opalski, in contradistinction to syphilitic vascular changes, in cysticercus endarteritis the internal elastica and the muscularis remain unchanged. However, Askanazy,[35] to whom belongs credit for identifying the vascular changes in cysticercosis, saw resorption of the elastica and granulation tissue in the media in this form of arteritis. Our case showed such changes in some of the larger arteries at the base of the brain. With lack of definite differentiating points between syphilitic and cysticercus arteritis one must rely for the determination of the nature of the lesions on the localized distribution of the arteritis in cysticercosis, in which the changes are more or less limited to the proximity of the cysts, while the syphilitic changes are more disseminated. In our case, in addition to the extensive endarteritis at the base of the brain, there was advanced endarteritis of the branches of the right middle cerebral artery, caused by a cysticercus in the right sylvian fissure; this cortical endarteritis resulted in a large cortical softening which was probably precipitated by the operative trauma, as it developed during the night following the operation.

The perivascular infiltrations, which were present in our case in the brain tissue at the base and along the ventricular surfaces, resembled miliary gummas. To exclude coexisting syphilis we stained the cerebral cortex for iron. This reaction, which was positive in our several cases of syphilitic meningitis, was negative in the case of cysticercosis. The microglia showed no rodlike arrangement.

Another cerebral lesion frequently mentioned in cysticercosis and observed in our case is granular ependymitis. This change has no differential diagnostic significance as it occurs in syphilitic and other diseases of the brain.

---

35. Askanazy, M.: Ueber die pathologisch-anatomische Wirkung der Hirncysticerken, Deutsche med. Wchnschr. **28**:431, 1902; in Aschoff, L.: Pathologische Anatomie, Jena, Gustav Fischer, 1911, vol. 1, p. 260.

The loss of eyesight in our case was caused clinically by a primary atrophy of the right optic nerve and by a secondary atrophy of the left optic nerve, which was the result of mild hydrocephalus caused by the exudate in the sylvian aqueduct and in the fourth ventricle. Microscopically both nerves showed chronic inflammatory and degenerative changes, apparently caused by the proximity of the cysticercus, which from the right sylvian fissure extended into the anterior fossa.

Prognosis.—The duration of cysticercosis of the brain is at times very long, as in a case of Guillain's in which the first manifestation of the disease (epileptiform attacks) appeared twenty-five years before death. Our case, with a total duration of one year and nine months, ran a rather rapid course. The ultimate prognosis is bad, as surgical intervention, the only possible means of removing the parasites, is not indicated in the early stage of the disease because of the vague symptoms and is resorted to only for the relief of intracranial pressure in the terminal stage when the lesions are numerous and severe.

SUMMARY

1. A case of meningo-encephalitis caused by a racemose form of Cysticercus cellulosae is described.

2. No tapeworm was found in the intestine of the patient at necropsy.

3. The parasite was identified by the structure of the cyst wall, as the body of the parasite could not be recognized with certainty.

4. For a time the patient showed pronounced eosinophilia, which later disappeared from the blood and from the cerebrospinal fluid.

5. The pathologic changes in the meninges and in the arteries were inflammatory. They were most pronounced in the proximity of the parasitic cysts.

6. In addition to the inflammatory changes there was a large zone of encephalomalacia due to a cysticercus endarteritis of branches of the right middle cerebral artery.

7. The optic nerves showed advanced inflammatory and degenerative changes.

ASSOCIATED MOVEMENTS OF TONGUE IN EPIDEMIC ENCEPHALITIS CONTROLLED BY VOLUNTARY EFFORT

MELBOURNE J. COOPER, M.D., PHILADELPHIA

The occurrence of abnormal involuntary movements as sequelae of epidemic encephalitis is well known. The most familiar of such movements are myoclonias, choreiform movements, disturbances of the respiratory cycle and oculogyric crises. Ornsteen [1] observed a variety of less common hyperkinetic signs in a group of cases of chronic epidemic encephalitis with parkinsonism. All of these movements were involuntary and occurred abnormally in association with one or another automatic movement pattern. Included in the group were: elevation of one arm so that the hand rested on the chest while walking in one instance, and similar elevation of both arms until the hands were placed on the occiput in another; akinesia of one arm and hyperkinesia of the other in walking; elevation of the left forefinger while using the right hand in writing, and synchronous deviation of both extended arms to the left, followed by transitory pill-rolling movements of the fingers (not seen at any other time) in association with a torticollis in which the head turned toward the right. One of the several patients in Ornsteen's group had a hemiparetic gait while walking but no sign of hemiparesis while running or while going up stairs. In cases similar to the one just mentioned, Brickner and Lyons [2] postulated a cortical representation of neuronic patterns for individually acquired skilled automatic associated movements (throwing and catching a ball, boxing, roller-skating, etc.) in contrast to the representation in the lower centers of more primitive patterns, such as those for walking. They believed that in their cases the individually acquired patterns dominated and were capable of inhibiting the phylogenetically grounded patterns, provided that the individually acquired patterns had been laid down before the onset of the disease.

The case reported here is unusual in exhibiting (1) marked involuntary protrusion of the tongue associated with talking and performing acts requiring complicated movements of the hands or deep mental concentration and (2) associated overaction of the flexor muscles of the right hip and knee in walking. It is of further interest in that these phenomena probably belong in the same category as those observed by Ornsteen and that they subsided in large measure coincidentally with the subsidence of the parkinsonian features and with continued conscious effort toward eliminating them from the movement pattern.

From the D. J. McCarthy Foundation, School of Medicine, University of Pennsylvania.

Read in abstract at a meeting of the Philadelphia Neurological Society, March 23, 1934.

1. Ornsteen, A. M.: Peculiar Arm and Head Movements in Chronic Epidemic Encephalitis, read before the Philadelphia Neurological Society, Dec. 19, 1930.

2. Lyons, L. Vosburgh, and Brickner, Richard M.: Physiologic Differences Between Teneric and Individually Acquired Automatic Associated Movements, Arch. Neurol. & Psychiat. **25**:998 (May) 1931. Brickner, Richard M., and Lyons, L. Vosburgh: Further Studies on Individually Acquired Automatic Associated Movements, Bull. Neurol. Inst. New York **2**:294 (July) 1932.

REPORT OF CASE

History.—K. W., a woman, aged 23, was admitted to the service of Dr. William G. Spiller at the Hospital of the University of Pennsylvania, complaining of difficulty in talking, involuntary protrusion of the tongue and stiffness of the right knee. At the age of 13 years she slept continually for three days and was partially somnolent for several more days. She noticed an awkwardness and stiffness of the right lower limb beginning six years after the period of somnolence, but the only effect of this was to make her awkward in playing tennis in contrast to her former agility. She stubbed the right toes while playing. About the same time that the spasticity appeared she noticed tremors of the hands, which were much more pronounced on excitement. Almost two years after the onset of the latter symptoms she suffered severe pain one night as a result of chemical cauterization of a callus on the right great toe, and on the following morning she first experienced difficulty in talking owing to involuntary protrusion of the tongue between the teeth and beyond the lips as she attempted to speak. Apparently at the same time there developed overflexion of the right hip and knee with each stride of the right lower limb in walking, so that the right knee and foot were raised unnecessarily and conspicuously high, with forward progression of the right foot.

These symptoms became gradually more pronounced. The patient was unable effectively to prevent the protrusion of the tongue as she talked, wrote or used the hands for any skilled movements, even though she made every effort to overcome the condition. As she articulated the first few words of a sentence she could by strenuous effort control the movement, sometimes even keeping the jaws clamped shut for this purpose. In a few seconds, however, she would lose this control. The strong voluntary efforts at inhibition resulted in a pronounced sense of fatigue and stiffness of the muscles of the throat, tongue and lips, making the patient most uncomfortable. Use of the hands in skilled movements or rapidly alternating movements, writing or any task requiring mental concentration was consistently accompanied by similar protrusion of the tongue.

The right limbs were relatively weak and stiff subjectively, and the patient quickly became fatigued on exertion of any form, the fatigue being uncomfortable, almost painful, as in the muscles of the throat and tongue. She had increased salivary secretion, and clonic twitching of the throat and tongue muscles probably had occurred at one time. Bright light shining into the eyes had at times caused involuntary upward rotation of the eyeballs lasting a short time. All of the symptoms were distinctly less marked in the first hours after awakening each morning, and were greatly increased by excitement of any sort and by worry.

The family history and the past medical history were without significance.

The patient's home environment had been agreeable to her prior to the illness, but since then it had become unsatisfactory. There were nine siblings; the home was small and inadequately furnished, and the father was an invalid as a result of an injury. The parents continually rebuked and criticized the patient, thinking that her symptoms were due to weakness of character and could be corrected by uncompromising discipline. The antagonism between the patient and her entire family, particularly the parents, increased steadily and became intolerable to the patient. At the time of admission to the hospital she had decided that she would never return to her home unless cured or greatly improved, as she refused to submit to further discipline at home. In fact, at one time when she feared that she would be returned home in spite of her protests, she threatened secret flight from the hospital or, failing in that, suicide.

There had been a short adolescent infatuation which apparently had ended painlessly. This was followed by a deeper affection for another man which began when the patient was 19 and promised to culminate in marriage as soon as the patient's health permitted. A detailed account of her attitude and reactions toward these two experiences and the men concerned, as well as the other circumstances of her career, revealed no sources of conflict which seemed significant, aside from the situation in her own family, which had arisen subsequent to the onset of the symptoms.

Examination.—The general physical condition was essentially normal. Neurologically, there was a mild grade of parkinsonism. The bodily attitude was mildly rigid, the facial expression was somewhat fixed, and winking was reduced in frequency. All movements were somewhat slow, and there were rapid, rhythmic tremors of the muscles of all four limbs and of those of the tongue and neck. The tremors were coarser and more pronounced in the right hand. The muscle tone was increased; in the right upper limb there was a suggestion of cog-wheel rigidity. The tendon reflexes were hyperactive on both sides in all four limbs. The pupils were unequal and reacted inadequately to direct and indirect light and in convergence. Convergence was much impaired.

The tongue deviated slightly to the left on protrusion and showed a fine, rhythmic tremor which was increased by excitement. The tongue could be moved voluntarily in all directions in a coordinate manner and protruded and retracted at will, and could be accurately directed by the patient so as to touch a cotton-tipped applicator held anywhere within its range of movement. No involuntary movements other than the tremors were seen except in association with speech, use of the hands or conscious mental concentration on a skilled act or problem. In the associated movements the tongue extended from 1 to 3 cm. beyond the lips, and although moving freely in articulation, its abnormal position interfered with clear enunciation of practically all the vowel and consonant sounds, especially the stopped consonants and the tooth-tongue consonants. The defect of speech closely resembled that of a tongue-tied person, though it was more pronounced. The interference with enunciation occurred only in a sequence of sounds, as in ordinary speech. Phonation for all single vowel or consonant sounds was normal, and in a single word of one or two syllables the combination of sounds was normally effected.

As the patient walked there was marked reduction in the associated swing of the right arm, and that arm was held in a semiflexed position. The right knee and hip joints were flexed excessively at each stride as the right leg was carried forward, the effect being an unusual elevation of the knee and foot. This could be prevented by conscious effort of the patient in holding the extensor muscles of the hip and knee in tonic contraction, so that the toes of the right foot were scraped lightly along the floor, as in a mildly hemiplegic gait. This could be continued only for about twenty steps, however, as the extensor muscles readily became fatigued.

Examination of the larynx with a mirror showed no limitation of movement of the laryngeal muscles and no local disease. The palate and pharyngeal muscles moved normally. The Wassermann and Kahn tests of the blood were negative; routine studies of the blood and urine revealed no abnormalities, and roentgenograms of the skull revealed a normal picture.

During the course of the investigations acute appendicitis developed, and an appendectomy was done. Convalescence from the operation was uneventful, and there was no apparent effect on the neurologic status.

Diagnosis and Course.—The conclusion reached was that the patient had postencephalitic parkinsonism. The movements of the tongue and legs were regarded as a part of the syndrome, of the same category as the involuntary flexion and abduction movements of the arms associated with walking that are occasionally seen in postencephalitic cases.. The ability of the patient to prevent these manifestations temporarily by voluntary inhibition or by innervation of the opposing muscle groups, or by a combination of these methods, made the prognosis seem

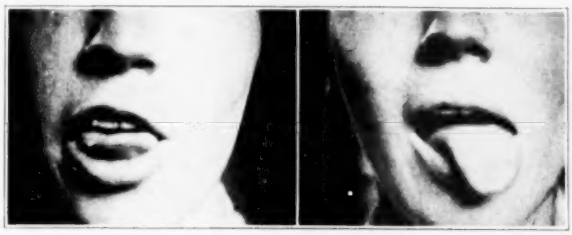


Fig. 1.—Enlargements from motion picture exposures taken during the course of conversation with the patient. The first exposure shows the beginning of an involuntary movement of protrusion of the tongue during enunciation. The second exposure, taken a moment later than the first exposure, shows the maximum protrusion and indicates the incoordinate and hyperkinetic character of the movement. Such movements recurred continually and rapidly but not rhythmically during conversation.

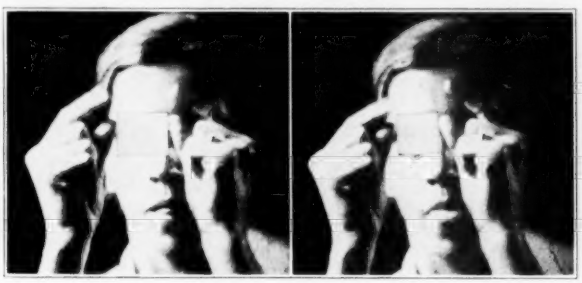


Fig. 2.—Enlargements from motion picture exposures taken during a voluntary skilled act of the hands (rapid repeated apposition of the tips of the forefingers to the tips of the thumbs). The first exposure shows the beginning protrusion of the tongue; the second exposure, taken a moment later than the first, shows further protrusion. Repeated, nonrhythmic alternate protrusion and retraction of the tongue continued during such movements of the fingers.

hopeful in some degree. The patient for many months had tried to overcome the speech defect more effectively by strong inhibition and by practicing slow and guarded speech with conscious pronunciation of each sound and syllable separately. She had carried out such attempts at reeducation earnestly, but they had not resulted in any appreciable benefit. The painful sense of stiffness and fatigue of the muscles which accompanied such attempts had not been overcome, and this

prevented continuous inhibition. The overflexion of the knee and hip had received little attention from a therapeutic standpoint.

At the University Hospital it was considered that the treatment of the patient should consist of two fundamental parts: (1) reduction of the muscular spasticity by the use of stramonium and (2) reeducation in the synergic use of the muscles of speech and the use of the lower limbs in walking as much as possible as soon as the muscles became more agile. After convalescence from the appendectomy the patient was appropriately instructed and discharged to the care of Dr. R. F. Leinbach for supervision of the treatment. At the time of discharge from the hospital the symptoms were unchanged.

For three weeks after she returned home she was kept under observation by Dr. Leinbach, and no improvement was detected. At the end of that time the administration of stramonium leaves and of scopolamine was begun, but no other changes were made in the type of attempted reeducation or psychotherapy, and no change in the home situation occurred. Shortly after starting the administration of the drugs improvement was noted, and it continued steadily. The average daily dose, determined by the patient's tolerance, was 7½ grains (0.5 Gm.) of stramonium leaves and 1/200 grain (0.3 mg.) of scopolamine hydrobromide. The spasticity, the sense of muscular fatigue and the tremors of the hands diminished greatly, and less than three months after the medication was started the patient was able to control the movements of the tongue and the right lower limb without experiencing much fatigue. Her own reports of the progress were enthusiastic. The tremor of the hands was greatly reduced, the involuntary elevation of the knee subsided in large measure, and walking and talking were not distinctly impaired. In her own words, "My tongue stays in my mouth all the time now. You remember three months ago, I could not keep it in my mouth. I am walking almost perfectly again." Dr. Leinbach in an independent communication confirmed the patient's favorable reports in detail and added that the general spasticity and the tremors were much less pronounced than they had been three months previously.

COMMENT

Disturbance in speech associated with a state of fixity of the muscles, with limitation of movement of the lips, face, tongue and pharynx, were noted as sequelae of epidemic encephalitis by Olkon.[3] In his cases the muscles of speech were spastic and became fatigued on use, and there was difficulty in phonation as well as in articulation. In the case reported here the patient likewise exhibited parkinsonism with spasticity and fatigue of the muscles, but the abnormal and excessive associated movement of the tongue, i. e., a disturbance of the normal movement pattern, was the factor causing the speech disturbance, and the spasticity evidently played its part secondarily in preventing continued voluntary control of the tongue and reeducation in speech movements. The general factors of abnormal muscular contractions and fatigue of the muscles used voluntarily in opposing such contractions applied equally well to the peculiar elevation of the knee in walking.

It is well recognized that patients having involuntary movements as sequelae of epidemic encephalitis can arrest the movements for a time by conscious inhibition. Duncan[4] found that this was characteristic of the patients with choreiform move-

3. Olkon, D. M.: Vocal Myasthenia of Postencephatic Origin, Arch. Neurol. & Psychiat. **24**:570 (Sept.) 1930. Olkon, D. M.: A Unique Type of Speech Disturbance in Epidemic Encephalitis, ibid. **27**:172 (Jan.) 1932.

4. Duncan, A. G.: Sequelae of Encephalitis Lethargica, Brain **47**:76 (Feb.) 1924.

ments in his series, and Turner and Critchley [5] noted the temporary success of voluntary inhibition of respiratory disorders in their cases. The ability of this patient to prevent the associated movements for a brief period, the increasing control of these movements coincident with the reduction of spasticity and of other parkinsonian manifestations and the relationship of the movements to familiar automatic movement patterns make it appear that the condition is properly classified as chronic epidemic encephalitis with unusual sequelae.

SUMMARY

A case showing unusual involuntary movements of the tongue associated with talking, skilled movements of the hands or mental concentration and a comparable type of abnormal associated movements of the right lower limb in walking has been described, and the condition has been classified as chronic epidemic encephalitis.

The movements could be controlled only to a limited extent by voluntary effort before reduction of the muscular spasticity and other parkinsonian features, but control was greatly improved after the administration of stramonium and scopolamine.

It is believed that the combined influences of a reduction of spasticity of the muscles and continued voluntary inhibition of the abnormal movements were responsible for the rapid improvement in this case, and that by conscious effort an alteration of the previously disturbed movement pattern was effected.

DISCUSSION

DR. W. G. SPILLER: The peculiar action of the right hip and knee probably was caused by the rigidity of the lower limb in parkinsonism and by the position of the right foot which the patient assumed to prevent the pain caused by the callus on the right big toe. She walked on the four small toes to avoid pressure on the big toe, and with the heel elevated. This caused some flexion at the knee and hip joint.

The protrusion of the tongue associated with skilled movements of the hands, as in writing and especially in any task requiring mental concentration, I have seen in normal persons, often associated with puckering of the lips. This may be explained by the fact that the cortical centers for the hand and face, especially the thumb and forefinger, are close together, and overflow of innervation is possible from the hand center to the face center, especially when inhibition of the latter is impaired.

As I talked with this patient from time to time and encouraged her to keep her tongue within the mouth while talking, she gradually became more able to do this for longer periods. As excitement increased the involuntary movements, it was important that she should be kept as free from excitement as possible. She had broken an engagement to be married, and her family had not a proper understanding of her condition, but in the University Hospital the environment was conducive to self-control.

The use of stramonium and scopolamine, I believe, would make inhibition of the undesirable associated movements more successful and lessen the rigidity. A dose of these two drugs given to a surgeon afflicted with parkinsonism and con-

5. Turner, W. A., and Critchley, M.: Respiratory Disorders in Epidemic Encephalitis, Brain **48**:72 (March) 1925.

siderable tremor of the hands enabled him to perform an operation without difficulty while under their effect.

The movements of the tongue were incoordinate movements associated with those of other muscles employed in speech; they occurred because the proper inhibitions of the complicated mechanism of speech and singing were impaired by the lesions of chronic epidemic encephalitis. Such incoordinate associated movements must be distinguished from coordinate associated movements, such as the making of a fist or the raising of the upper limb when this limb is paralyzed in hemiplegia for voluntary innervation but responds in associated movement when the corresponding parts of the normal upper limb are voluntarily innervated. These associated movements are accomplished through the ipsilateral pyramidal tract.

DR. M. J. COOPER: The improvement in the patient's condition after three months was not confined to a reduction in the severity of the involuntary movements. There was decrease of muscular rigidity, of tremor and of the other manifestations of parkinsonism, brought about, it is assumed, by the effect of the stramonium preparations. The improvement was first evident shortly after the beginning of this treatment. The home environment and the routine of the patient's daily life have undergone no change since the patient's return to her home.

Dr. Spiller's insistence on the continued conscious attempt to inhibit the overaction of the tongue and the lower limb impressed on the patient the importance of reeducation and enhanced the form of psychotherapy which had been used for some time without effect. My associates and I believe that the psychologic factors influencing the patient were not changed in any other way.

Dr. Spiller's mention of the proximity of the cortical representation of speech and that of movement of the right hand is interesting. I have not ventured an anatomic explanation of the symptoms in this case. Turner and Critchley (*Brain* **48**:72 [March] 1925) attributed the respiratory disorders in their cases to a derangement of the involuntary psychomotor control of respiration, which normally is maintained, they hold, by corticopontile pathways. They placed the lesions at levels higher than the so-called respiratory centers. Brickner and Lyons (*Bull. Neurol. Inst. New York* **2**:294 [July] 1932) cited cases illustrating the apparent domination of the neokinetic patterns for skilled acts which had been acquired prior to the onset of dystonic symptoms and their power of inhibition of the more primitive paleokinetic patterns of movements. Assuming that in our patient the paleokinetic movement patterns were disturbed as a part of the parkinsonian picture, it may be conceivable that with the reduction of the symptoms of parkinsonism the cortical influence again gained precedence on conscious effort, permitting the patient to build up and strengthen a neokinetic pattern capable of controlling these movements. There is no basis other than analogy for such a conclusion in this instance, however, and in the cases of Brickner and Lyons the neokinetic patterns were acquired prior to the onset of symptoms rather than later.

NOTE.—A letter from the patient dated Nov. 8, 1934, states that she now has entire control of her tongue; she talks as distinctly as she has ever done, and her gait is so improved that little that is abnormal can be detected.

SPECIAL ARTICLES

A HALL OF NEUROLOGIC FAME

The biographic sketches of Cajal and of Golgi which appear in this number of the ARCHIVES inaugurate a series of biographies of famous neurologists.

Thirteen panels in the frieze of the entrance hall of the new Montreal Neurological Institute are inscribed with the following names:

Hughlings Jackson

Victor Horsley

Charles Sherrington

Jean Charcot

Claude Bernard

Constantin von Monakow

Wilhelm Erb

Franz Nissl and Alois Alzheimer

Ivan Pavlov

Ramón y Cajal

Camillo Golgi

Weir Mitchell

Harvey Cushing

Members of the staff of the Montreal Neurological Institute have written biographic sketches of these men in connection with the inauguration of that institution. With the possible exception of the living members of this group, the biographies will appear in succeeding issues of the ARCHIVES.

SPECIAL ARTICLE

SANTIAGO RAMÓN Y CAJAL
1852–1934

WILBUR SPRONG, M.D.†
MONTREAL, CANADA

Santiago Ramón y Cajal was born on May 1, 1852, in Petilla, an isolated village in the Pyrenees. Both parents were sturdy native Aragonese. The father was a man of unusual ambition and ability who was not to be satisfied with his hard-earned status of "surgeon of the second class." Accordingly, he soon left Petilla and his peasant practice, completed a course in medicine and moved his family to Zaragoza, where he finally became professor of anatomy in the university. Such capacity and such an example were the heritage of Cajal.

His own grim experience with poverty and obscurity, as well as his natural disposition, made the elder Ramón very ambitious for his son, for whom he early prescribed a classical education and a career in medicine. But young Cajal had interests of his own. He loved to draw, and he wanted more than anything else to become an artist. Samples of his efforts before the age of 10 are preserved, and they leave no doubt that he had exceptional talent, that he was a born morphologist. He was an ardent collector of birds and their nests. He played at war, experimenting with arrows and formulating a science of ballistics of his own. If one of his father's chickens strayed too temptingly into the open, it fell a prey to his artillery. Energetic, intensely absorbed by occupations of his own choosing, obstinate and self-willed, Ramón was the sort of lad to give grave concern to an oversolicitous parent.

Cajal's early schooling was of the worst sort. It began in a boys' school at Jaca, where he was subjected to an actual "reign of terror." He had a strong distaste for memorizing, and that unfortunately was the sole curriculum. So he was pronounced stupid and flogged repeatedly, and his childish nature was ruthlessly insulted. He became defiant, not docile. As a last resort, he was deprived of food to improve his scholarship, and at the end of five months he returned home a horrible picture of emaciation. But even the "reign of terror" could not spoil his sensitive eye for beauty. In his autobiography Cajal denounced bitterly such intimidation of youth but proceeded to enlarge with great sentiment on the scenic beauty of the fertile mountain valley around Jaca, which he found time to explore.

† Deceased.

After a rapid convalescence he was soon back at his childish warfare on a grander scale than ever. He decided to construct a real cannon, which admiring associates gathered from far and near to see. It went off, however, with such a disturbance that young Ramón was placed in jail for three days with the consent of his stern father, who further specified that he be deprived of food. His more sympathetic mother fortunately came to his rescue and slipped food into the dingy cell.

Who could perceive in his boyish activity the *Anlagen* of the adult career of Ramón y Cajal? Indeed, to his dominating father and misguided teachers he was a "problem child!" Most promising perhaps were a natural inquisitiveness and a stubborn will so hardy that they could withstand the worst form of pedagogy.

A year after the experience at Jaca, a school at Huesca was tried, where he did no better. So he was apprenticed to a barber and then to a shoemaker. At the latter trade, he became quite skilful. After a year of apprenticeships he returned to Huesca for another trial, but soon he was so unhappy that he tried to run away.

At this point the elder Ramón took charge of the boy's education, starting him on the study of osteology at home. Material for study had to be obtained by gruesome visits to a cemetery. The morphology of bones captured his interest at once and offered at last an opportunity to draw. He thrived as never before. After three years the results were so promising that the father, now professor of anatomy at Zaragoza, planned to publish an atlas of the drawings of his 17 year old son. Unfortunately it was impossible to obtain satisfactory reproductions in Spain at that time, and the work was never published.

Cajal then entered on a medical course at Zaragoza, giving a share of his time to varied side interests. For example, he worked diligently in gymnastics and became proficient. His romantic inclinations, which blossomed in this era, brought at least one welcome opportunity to try his strength in combat. On a certain street lived a young woman with large blue eyes and a beautiful figure, who because of her classic features was known to students as "Venus de Milo." The future Nobel laureate was frequently attracted to that street. On one occasion he encountered there an engineering student who was well known for his pugnacity, and Cajal was sternly ordered never to be seen on that street again. A memorable battle followed in which the young medico put his diligently acquired strength to good use and emerged the victor.

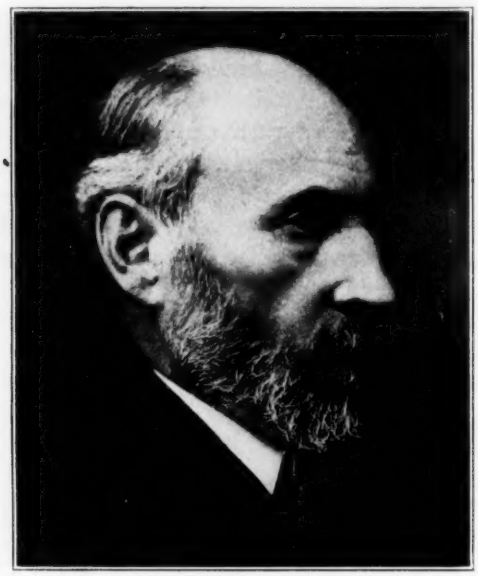
Without distinguishing himself as a student, he received a medical degree in 1873. Because military service was compulsory, he immediately joined the medical corps of the Spanish Army. After an eight month campaign at Lerida, he was promoted to the rank of captain and ordered to Cuba. Life in the tropics was a sad disappointment. Assigned to a crowded, unhealthy infirmary near Puerto Principe, he

soon succumbed to malaria and dysentery and never completely recovered until he secured his discharge in 1875 and returned to Spain.

After taking a medical degree at Madrid, he became a demonstrator and then, in 1877, professor of anatomy at Zaragoza. The next year, however, a grave hemoptysis announced the presence of pulmonary tuberculosis. This necessitated a long course of outdoor sunlight treatment, wisely prescribed by his father.

In 1879, on an income of 35 duros a month and against unanimous advice, Cajal married. He gave the following account of his decision:

> Returning one evening from a walk to Torrero I encountered a young girl of modest appearance accompanied by her mother. Her blushing, spring-like face



SANTIAGO RAMÓN Y CAJAL
1852–1934

> suggested Raphael's Madonna, or better still, a German colored engraving of Marguerite in Faust. Attracted no doubt by the sweet pleasant disposition apparent in her features, her slender figure, her large green eyes veiled by long lashes, her abundant hair, I was even more impressed by the air of childlike innocence and melancholy resignation that emanated from her whole being. Unseen, I followed the young girl to her home, learned that she was the orphan daughter of a modest employee and enjoyed a reputation for honor, modesty and domestic tastes. I made her acquaintance and, after a time, against the collective advice of my family, married her, not without due consideration of the mental characteristics of my fiancée, which were complementary to my own. My resolution was discussed by acquaintances in clubs and cafés as an act of madness: poor Ramón is lost forever. Goodbye to study, science and generous ambitions.

And yet, though eulogies do not flow readily from my pen, I take pleasure in saying that, with beauty which seemed predestined to shine in promenades, visits and receptions, my wife cheerfully condemned herself to the obscurity of my lot, remaining simple in her tastes and with no other aspirations than tranquil contentment, order and system in the management of the home, and the happiness of her husband and children.[1]

In 1884, Cajal was called to the chair of anatomy at Valencia. As a result of an epidemic of cholera, he was drawn for a time into the field of serology and bacteriology, where he made a promising beginning. But he turned to histology, and in 1887 was given a professorship in that subject at Barcelona.

Cajal was then 35. It was an odd and devious training that destiny had prescribed for him so far: a rude schooling in which he was thrice pronounced a failure, apprenticeships in barbering and shoemaking, transient flings at sundry hobbies, army life in Cuba, a rest-cure for tuberculosis and a succession of rather obscure university appointments. He had never seen one of the great investigators of his day. Isolated by language and tradition from the main current of science, he had grown and ripened in Spain, in the leisurely tempo of life in Latin countries. In retrospect, one can see in him at this point a striking figure. He was on the eve of an epoch of single-handed contribution probably unsurpassed in the history of medical investigation.

The young professor had already learned of the Golgi chrome silver stain from Dr. Luis Simarra, a neuropsychiatrist of Madrid. But Simarra, like many another worker, finally abandoned the capricious method. Cajal's first important result was an improvement of the Golgi stain, which placed in his energetic hands the very tool he needed. He at once began working systematically through the entire nervous system, staining its cells as never before and recording what he saw with skilful illustrations of his own.

This work attracted some attention in Germany, but the great German histologists had had disappointing experiences of their own with the Golgi stain and naturally doubted such success by an unknown Spaniard. So, in 1889, Cajal determined to demonstrate his work before the German Society of Anatomists, where he appeared in the august presence of His, Retzius, von Kölliker, Waldeyer, van Gehuchten, Bardeleben and Schwalbe. His hosts were properly dubious, but his preparations of nerve fibers of the molecular layer of the cerebellum, the ascending and descending branches of sensory nerves and the terminations of retinal fibers in the optic lobes of birds spoke for themselves. Von Kölliker at once gave him whole-hearted praise, a signal victory in itself. The work was soon accepted and confirmed by the entire German school of histology. Cajal's reputation was made.

1. Translated by Garrison, F. H.: Bull. New York Acad. Med. **5**:490, 1929.

Acceptance abroad was followed by appreciation at home. In 1892 he was called to the chair of "normal histology and pathologic anatomy" at Madrid. From now on one country after another showered on him its highest honors. In 1894 came an invitation to give the Croonian lecture before the Royal Society of London. Oxford and Cambridge conferred honorary degrees on him. In 1899 he participated in the decennial celebration of Clark University. In 1900 came the "Moscow prize" at the International Medical Congress in Paris, and in 1904, the Helmholtz medal of the Royal Prussian Academy. In 1906 he was awarded the Nobel prize at Stockholm, conjointly with Golgi. On this occasion his fellow prizeman conspicuously ignored not only the contributions of Cajal but of every one else, claiming for himself full credit for the development of the finer anatomy of the nervous system, to the consternation of the courteous Retzius and other distinguished guests. Cajal, in contrast, took full advantage of the occasion for a generous evaluation of the work of a host of colleagues who had stimulated and enlarged his own findings. Speaking in French, he said:

> Scientific discoveries are nearly always the result of intellectual environment, a collective labor in which it is often difficult to evaluate the part of a particular scholar. The "Institut Carolin," inspired by a lofty ideal of justice and equity, has well wished that one of the joint recipients of the Nobel Prize for Physiology and Medicine might be the illustrious Golgi, the renowned Italian master, who by very important research methods and a scrupulous and exact spirit of observation has made the greatest contribution to knowledge of the finer structure and functional mechanisms of the central nervous system. Nevertheless, other scholars have collaborated most actively in the common labor, and if you find in the regulations of the Nobel institution an insurmountable limitation to your generosity and sense of justice, I should be guilty of a grave injustice if I did not recall at this time the glorious names of His, the brilliant and lamented embryologist of Leipzig; of Forel, the learned Swiss naturalist and neurologist; of von Kölliker, the venerable master, the sage of microscopy, whom death alone could stop in the struggle by which he has wrested so many secrets from living nature; of Ehrlich, Marchi and Weigert, creators of important methods of neurological research. Nor do I forget the legion of young and brilliant professors such as van Lenhossek, Dogiel, Lugaro, van Gehuchten, Held, Edinger, Fusari, L. Sala, Holmgren and others; and finally one of your most prolific and untiring investigators, the illustrious anthropologist, histologist and embryologist, to whom the comparative anatomy of the nervous system is indebted for great and positive conquests. I refer, as you no doubt realize, to Professor G. Retzius of Stockholm.
>
> All of these scholars merit equally the great honor that I am happy to share to-day with the master of Pavia, because, in addition to their own original investigations, they have all contributed by suggesting, preparing and developing many important points in my modest discoveries.

Such coronations, however, were only brief distractions from the laboratory. Cajal was an inspired genius, but above all a faithful workman. On coming to Madrid at the age of 40, he established a regimen of living that permitted forty odd years more of intensive,

sustained activity. Prominent in this regimen were certain simple diversions, such as frequent walks through the beautiful environs of Madrid and regular "tertulias" with friends at a favorite café.

Even in moments of diversion from the laboratory, he was seeing many things worth recording. His varied life is recalled in a volume of memoirs (1901-1917). Excursions with a camera through the country gave rise to a treatise on color photography (1912). Reflections over the coffee cups in his favorite café became the substance of a book entitled "Coffee-House Chatter." This is a collection of anecdotes and aphorisms concerned with the features and foibles of man, tolerant but with few illusions, often embellished with delightful humor.

His recorded scientific work is a towering intellectual monument. By prodigious industry, happily continued over a long period of years, he had published 237 scientific papers when his autobiography was revised in 1923. In addition, he wrote an imposing collection of comprehensive volumes: a treatise on the "Texture of the Nervous System of Man and the Vertebrates" (1897-1904) in three volumes, with a revised edition in French, "Histologie du système nerveux" (1909-1911) in two volumes; "Degeneration and Regeneration in the Nervous System" (1913-1914) in two volumes and 11 other books. In the last ten years of his life he added compilations and correlations of his earlier work. The crowning achievement is, perhaps, the "Histology of the Nervous System." These volumes give classic pictures and epochal conceptions of cell structure in every part of the nervous system. To peruse their pages is research. Indeed, years from now investigators unfamiliar with them will no doubt continue to rediscover what Cajal found at the turn of the last century.

Even more lasting than his wealth of recorded observations will be the improved methods of Cajal and his disciples. First, in 1888, he increased the applicability of the Golgi stain. In 1903 he developed his own reduced silver nitrate stain for nerve cells and nerve fibers. In 1913 he introduced the gold sublimate stain for astrocytes which at the same time enabled him to describe a "third element" in the nervous system. Special adaptations of Bielschowsky's method by his eminent pupils Achucarro and Hortega yielded the silver carbonate stains, giving such improved pictures of the "third element" that both microglia and sensitive oligodendroglia were at once placed under the observation of histologists and pathologists.

These methods, in the hands of Cajal and his students, have clarified much of the embryology of each cellular element in the nervous system. Furthermore, the finer details of gliomas revealed by these stains, with the accumulating light from embryology, have given to the neurosurgeon useful correlations of structure and biologic characteristics of brain tumors.

Cajal at 82 still labored in a modest laboratory in his home. His inquisitive spirit and exacting methods have been imparted to a celebrated Spanish school of histology. Among his immediate disciples are such eminent investigators as del Rio Hortega, the late Nicolas Achucarro, Tello, de Castro, Villaverde, Sanchez and his own son, Ramón Fananas. On a hill in Madrid stands a magnificent institute named for Cajal. The leaven is evident in every Spanish speaking country. With prophetic vision and charming simplicity, he wrote this precept and made his life its finest example:

> It has been said many a time that the problem of Spain is a problem of culture. It is necessary in fact, if we would enroll ourselves with the civilized peoples, that we must cultivate intensively the desert of our land and brain, thus rescuing by prosperity and mental vigor all those national riches that have been lost in the sea, and all those talents which have been lost in ignorance.[2]

NOTE.—Wilbur Sprong, the author of this biographic sketch of Cajal, died on Nov. 23, 1934. The reader of the biography will recognize Sprong's power of expression, and he may sense the author's youthful enthusiasm and quick insight, but he can scarcely surmise the clinical and scientific ability which was obvious to all who knew this promising young neurosurgeon.

---

2. Translated by Penfield, W.: The Career of Ramón y Cajal, Arch. Neurol. & Psychiat. **16**:213 (Aug.) 1926.

CAMILLO GOLGI

1843-1926

JERZY CHOROBSKI, M.D.
MONTREAL, CANADA

The nineteenth century not only reflected changing aspects, political and social, but saw the foundations laid for many of the branches of modern science. In Italy it was the century of national renaissance, replete with far-reaching achievements in the field of biology and medicine. These were initiated by Spallzani's experimental researches dispelling the clouds of vitalism and of humoral theories and by the accurate anatomic studies of Malpighi, Morgagni, Scarpa and others. In Pavia, men like Tomassi, Panizza, Porta and Hoel ardently taught the necessity for placing the whole of medicine on sound anatomic and physiologic foundations.

At that period in the history of Italian medicine there entered on the scene an unassuming and retiring young man who aspired chiefly to obtain a professional education but whose brilliant mind, great tenacity and enthusiam for work carried him later to the greatest success in science and in medicine. He believed that "one obtains a positive scientific experience not through phantasy, which leads only to an appearance of progress, but through a methodical, careful, daily research, which, while leading to an accurate knowledge of particular facts, unveils the real basis for an understanding of the laws of life." Henceforth his life was that of daily, hard and toilsome striving toward realization of such an ideal. Some of the glorious results of his work are contrary to accepted scientific opinion, yet they are of such great brilliancy and stimulating value that he is acclaimed and honored throughout the world. His name is counted among the illustrious.

Camillo Golgi, son of a distinguished practitioner, was born on July 7, 1843, in Corteno, an Alpine village in the valley of Camonico. He studied medicine in the small medieval city of Pavia, which became for him the city of election and which he refused to leave all his life. Graduating in 1865, Golgi presented as his thesis a work in which he discussed with great precision and criticism the possible causes of mental disorders and pointed out the necessity for classifying such disorders according to anatomic and etiologic factors. His professional career began at the Ospedale di San Matteo in Pavia, where he remained until 1872. During those six years Golgi frequently visited and worked in the institute of general pathology, directed first by Mantegazza, its

founder, and later by Bizzozero. In 1868 he was assistant to Cesare Lombroso in his Clinica psichiatrica.

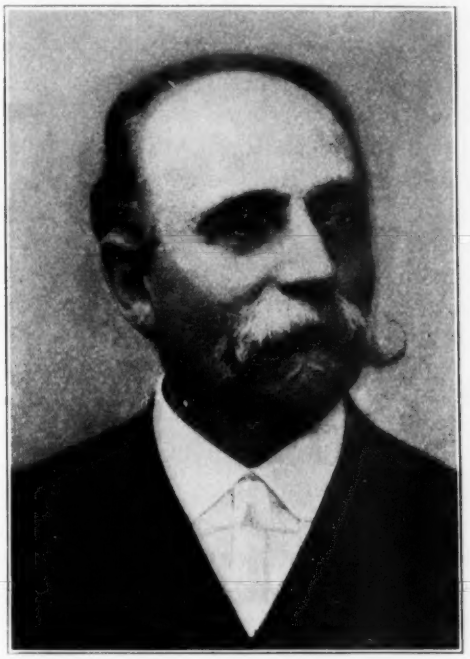
Fantoni's pessimistic views on "the obscure texture, the more obscure diseases and the most obscure functions" of the nervous system, although two centuries old, were still held during Golgi's early years. Influenced greatly by Lombroso's tendency to reduce psychiatry to a positive science and by the reading of Virchow's "Cellular Pathology," and initiated by Bizzozero into the methods of histologic investigation, Golgi decisively chose his course for the rest of his life: the study of the microscopic anatomy of the nervous system as an approach to the understanding of its function.

Some of Golgi's early work is thought to have been planned, if not actually written, at Lombroso's suggestion, and it was from the latter's clinic that he published his first paper, the clinical history and autopsy findings in a case of pellagra (1868). In this he observed that "the perivascular lymphatics of every region of the brain were filled with granulo-adipose cells." From Bizzozero's laboratory came a publication on psammomas (1869) in which Golgi stated for the first time that these tumors are of endothelial origin, without, however, excluding the possibility that fixed connective tissue elements may enter into their composition. Also under Bizzozero's influence, Golgi described the perivascular spaces of the brain (1870) as they are known at present, pointing out the important rôle which they play in the dissemination of secondary neoplasms of the brain, and showed that the perivascular spaces of His are artefacts due to shrinkage of the brain tissue.

By simple dissociation methods and from sections made by hand of material hardened in solutions of potassium bichromate or osmic acid, Golgi was able to describe clearly the neuroglia of the cerebral gray and white matter (1870, 1871) and later that of the retina of the horse (1872). He showed that it consists of cells of various sizes, provided with a roundish and somewhat eccentric nucleus and a lamellar cytoplasm which continues into a number of very delicate processes. Many of them, stated Golgi, are to be seen directed toward a blood vessel on which they end by means of small expansions "either directly on their walls, if they are capillaries, or on their lymph-sheath, if they are of greater dimensions." These observations, on the whole, are similar to those obtained with modern methods of investigation.

Economic circumstances obliged Golgi to accept in 1872 the post of chief resident physician and surgeon in a hospital for incurable patients in Abbiategrasso. Here, cut off from every form of scientific activity, his laboratory consisting of a microscope and of a few instruments collected in the kitchen of his home, working evenings by candle light, he discovered his epoch-making silver chromate method, "la reazione nera."

This method, although at first viewed by some with great reservation and called the method of the silhouettes, was accepted soon so enthusiastically that it was said that by means of it "on arrivera à Golgifier les pommes de terre" (one will eventually Golgify potatoes). It produced a revolution in the conceptions of the microscopic structure of the nervous system. Ramón y Cajal described the results of its application in the following terms:



CAMILLO GOLGI
1843-1926

. . . Against a yellow background of a perfect translucidity, appear scattered black filaments, smooth and thin, or thick and thorny, black bodies, triangular, starlike, fusiform! One would say drawings of china ink on a transparent papier du Japon. The eye, accustomed to the inextricable network of the carmin and hematoxylin stained slides, upon which the mind strives to attain marvels of criticism and interpretation, always in suspense, is confused. Here, all is simple, clear, without confusion. There is no need to make interpretations; one has only to look and ascertain . . . Amazed, the eye cannot detach itself from such a contemplation. . . .

With this method at hand, Golgi studied the minute anatomy of the cerebrum, cerebellum and spinal cord, with special attention to the cerebellum, cornu ammonis and the olfactory system.

He first briefly mentioned his method in 1873 and in 1874 in two papers which contained some of the fruits of its application. In the first of these he gave his original description of the two main types of nerve cells, which are now frequently referred to as Golgi's type I and type II, the long and short axon nerve cells, respectively. Protoplasmic processes of both types terminate by means of free extremities. The axon of the first type leaves the gray matter and, retaining its individuality, continues toward the periphery as the axis-cylinder of a medullated fiber. The axon of the type II cell terminates in a very complicated way in the gray matter itself and loses its individuality by forming an extensive terminal arborization. These observations have been many times confirmed and are now unanimously accepted. Pointing out, however, that the axon of the type I cell "is not simple," but provided with collaterals giving origins to others "with the consequent formation of a complicated system of filaments everywhere diffused in the cerebral gray matter," Golgi made the first step toward his conception of a rete nervosa diffusa. He believed that this was composed of the terminal arborizations of the collaterals of the type I cell axon and by the whole of the axon of the type II cells. This interpretation, which he placed on the facts observed by him, was attacked and disproved later by many.

In the second publication he described the large nerve cells of the granular layer of the cerebellum, which therefore are named after him, and pointed out that almost all of the small elements of the molecular and granular layers of the cerebellum are nerve cells.

There followed a study in which he showed, by applying his new method for the first time to a histopathologic problem, that chorea is not due to a mere functional disturbance but is associated with definite lesions in the central nervous system (1874). Working on this case led Golgi to describe also the calcareous degeneration of nerve cells—a subject dealt with extensively in a subsequent paper (1876). To the same period belongs his contribution to the knowledge of gliomas of the brain (1875) in which he demonstrated the reproduction of the neuroglia. He specified also the distinctive histologic characteristics between sarcomas and gliomas, generally confused with each other at that time, and commented on the practical value of such a distinction, as the gliomas do not metastasize and therefore should be considered as malignant tumors only from a local point of view. While still in Abbiategrasso, Golgi gave his first description of the structure of the olfactory bulb (1875), to which problem he returned some years later (1882).

In appreciation of the value of his important contributions to the knowledge of the anatomy of the nervous system, Golgi was called to

Pavia in 1875 as associate professor of histology. The same year he competed for and obtained the chair of anatomy in the University of Siena, but he left this some months later to return to Pavia as professor of histology. He was then given a laboratory, a small room in a sort of a garret in the Botanical Garden, and although in 1881 he was made full professor of general pathology and histology, it was not until 1894 that he finally succeeded in obtaining a real laboratory. After his retirement in 1918, he continued to teach histology in a free course till almost the end of his life. In Pavia, Golgi continued his work on the histology of the nervous system and also made fundamental contributions in the field of general pathology.

In 1885-1886 his monumental work appeared, "Sulla fina anatomia degli organi centrali del sistema nervoso" (U. Hoepli, Milan), which consisted of many of the papers published previously, in instalments, in the *Rivista sperimentale di freniatria,* a journal of which Golgi became co-editor. The volume, divided into eight parts and illustrated by magnificent plates made from Golgi's original drawings, was reprinted in French in the *Archives italiennes de biologie* and, with the addition of some previous and subsequent papers, was translated into German and published in Jena, in 1894, by G. Fischer. In English the work appeared in the 1883 and 1885 volumes of the *Alienist and Neurologist,* translated by J. Workman. In the last chapter, dealing with methods of investigation, Golgi gave the detailed description of his slow and rapid processes and of his bichromate and mercuric chloride method.

In this work, in addition to the presentation of his histologic observations, he added two suggestions: The first regarding the possible relationship to motor and sensory function of the type I and type II cells, respectively, a relationship which Golgi did not consider, however, as being proved and to which he did not attribute much importance. The second dealt with the trophic function of the protoplasmic processes of nerve cells, but he also insisted (in Stockholm, in 1906) that this did not mean the exclusion of these processes from the specific function of nerve cells of which they are mere expansions.

Here he emphasized also his critical attitude toward the conception of the isolated course of nerve fibers, as postulated by the neuron theory, and toward the possibility of delimitation of definite functional cortical areas. From his microscopic observations, made by means of his method, he felt that once within the central nervous system the nerve fibers, both efferent and afferent, lose their individuality, breaking up into a number of secondary rami or giving off fine collaterals which in turn ramify in the adjacent nerve substance. Owing to this anatomic peculiarity and to the mode of branching both of the axons of type II cells and of the collaterals of the axons of the type I cells, the gray matter of any given region of the central nervous system is composed

of a network of nerve fibers to which no definite boundaries can be attributed. These nerve fibers may be related to extensive groups of nerve cells to which, in addition, there may be related a number of fibers having different destinations and possibly different functions.

Golgi insisted that in such a fine network, in which the constituent filaments are so closely situated and have frequent and extended contacts, direct continuity is not necessary for the transmission of nerve impulses from one to the other. Considering the existence of his rete nervosa diffusa as a definite histologic entity and not merely as a working hypothesis, he persistently refuted the neuron theory. His views on that problem were expressed in part in 1902, in a letter to Luciani, and more extensively in his lecture at Stockholm, in 1906, on the occasion of receiving, jointly with Cajal, the Nobel prize. He felt "that the neuron theory is a word which has its fortune especially through the authority of him who put it in use, Waldeyer, but it cannot show the founded rights to durable citizenship in science," and he considered Cajal's law of conduction or of dynamic polarization "as one of the explanations of the way of functioning of nerve elements—which should not, however, be used to the exclusion of others."

If, as is known, the work of Cajal, Lenhossek, Edinger, Held, van Gehuchten, Retzius, Lugaro and a legion of others who used Golgi's own method has cleared away his erroneous belief in the rete nervosa diffusa, Golgi's credit for discovering a method permitting an accurate investigation of the nervous system and for his contributions to the morphology of the nerve cell will last forever.

To his work on the histology of the nervous system two other important discoveries of Golgi belong, namely, the description of the "musculotendinous end-organ" thought by him to play a rôle "in the regularization of the muscular effort required to overcome a definite resistance" (1880) and the discovery of the "apparato reticulare interno" (1898). Golgi realized promptly the general value of this discovery, and by showing (1909) that in certain epithelial cells the apparatus may become shifted from the ordinary position he anticipated the results of more recent investigations regarding the important part that the cell organ probably plays in secretion. Whatever will be the final judgment on the meaning and morphology of the reticular apparatus, Golgi's credit in describing this cytologic structure will always be great indeed.

From his numerous and important contributions in the field of general pathology, two must be mentioned specifically. In the first, Golgi corrected the erroneous conception of the structure of the kidney generally held in his time. By a simple maceration method and by employing embryologic data to explain anatomic arrangements characteristic of the adult state, he showed the exact course of uriniferous

canaliculi and the relation of their different portions to one another and to the renal glomeruli (1889).

The other contribution, Golgi's second epoch-making gift to science besides the work on the nervous system, was his brilliant research on malaria. Five years after Laveran discovered the parasites of malaria in the blood, Golgi from simple smears of fresh blood gave a masterly description of the plasmodium of the quartan, and later of that of the tertian, fever and of their nonsexual development (1886). By showing that the beginning of fever in malaria coincides with the sporulation phase, taking place at intervals definite for each species of the parasite, and by demonstrating the destructive properties of quinine on the plasmodium, he led the way to the rational treatment of this disease. Golgi described also the quotidian fever and believed that it might be due to a double infection with the tertian plasmodium, each group sporulating on successive days—an observation soon confirmed by other workers. The first photograph of Plasmodium malariae was shown by Golgi in 1890, and three years later the estivo-autumnal type of malaria was described by him as a separate entity.

Golgi did not cease to work, however. His last publication appeared three years before his death, at the age of 80. Describing the results of his investigations on yolk spheres, chiefly on those of frogs' eggs (1923), he observed that the yolk spheres, if examined in spring and in the succeeding months, may under certain conditions present histologic appearances (centrosome, mitochondria, etc.) which are generally regarded as proper to living elements alone.

All of Golgi's papers published between 1868 and 1902 were reprinted in 1903, in three volumes, by U. Hoepli in Milan, as his "Opera omnia." Only 325 copies were issued. The bibliography of his subsequent papers has been given by Da Fano in his obituary of Golgi in the *Journal of Pathology and Bacteriology*.[1]

During his life, Golgi was known to have had three great passions. The first was for his family, personified by his wife, Donna Lina Golgi, who survived her illustrious husband and who was the niece of his admired and beloved friend Giulio Bizzozero, and by Aldo Perroncito, his nephew and adopted son, who succeeded Golgi in 1918.

His second great love was for his laboratory where he used to spend most of his time, finding there solace and joy in the constant pursuit of scientific problems. He, who during his most brilliant discoveries was almost entirely without means of investigation, did not tolerate that others should lack the possibility to attempt all the available methods of study, and it was his greatest care to obtain for the institute now bearing his name great liberality of means. Although firmly convinced

1. Da Fano: J. Path. & Bact. **29**:1926.

that histology should be considered as an indispensable instrument for proper understanding of the laws of normal and pathologic life, he always emphasized that other methods of investigation should not be neglected. For that reason Golgi kept the (honorary) direction of a hospital department almost all his life, so that he and his pupils might maintain the bonds uniting science with the practical side of medicine.

Golgi's work was at first unnoticed, but as soon as it became widely known many pupils from Italy and from abroad crowded his laboratory. There, to mention only a few, Negri was demonstrating his cell bodies occurring in rabies, a subject in which Golgi was actively interested himself. There worked Fridtjof Nansen, who later became famous in the camp of Golgi's opponents, supporting the neuron theory. There another distinguished opponent of the rete nervosa diffusa spent some time, Albert von Kölliker, Golgi's lifelong friend and admirer.

The third passion of Golgi was his deep attachment to the University of Pavia, of which he was twice rector. It was his great ambition to keep his alma mater forever as the center of high education and research of his native Lombardy, and he was greatly interested in the rise and organization of new clinical institutes.

Of gentlemanly austerity, extremely modest and reserved, courteous to everybody, endowed with a great intuition and an accurate power of observation, Golgi presented brilliant intellectual aptitudes as a scientist which were equal to the nobility of his character as a man. A member of the Superior Council of Public Instruction and Sanitation, the teacher was not less than the scientist. A member of many foreign medical societies, receiving numerous scientific prizes and honors, Golgi, a great patriot, took also an active part in many of the political institutions of his country, being a member of the Royal Senate for several years. In his late years a great amount of Golgi's energy was spent in defending his scientific ideas, sometimes cruelly attacked. His friends have often seen him suffer profoundly from disillusionment because of the defection of pupils whom he thought faithful, but he never permitted himself to give external manifestations of his thoughts and feelings. He considered and admired highly the greatest of his opponents, Ramón y Cajal, and he manifested his esteem for him in writing. He never permitted himself to be disturbed in the continuity of his labor, and it seemed that the faith and the passion for research never grew less in him.

When he died in the beautiful Casa Golgi in Pavia in January 1926, Italy lost one of its greatest citizens, medicine a leading scientist and distinguished teacher and his associates and pupils a tender and affectionate friend.

Ottorino Rossi, bidding Golgi his eternal farewell, spoke of him: "Gloria gloria, a Te o immune della morte. . . ."

News and Comment

CENTRAL NEUROPSYCHIATRIC HOSPITAL ASSOCIATION

The Central Neuropsychiatric Hospital Association, which was founded in 1927, was organized to foster the development of adequate medical and administrative standards in private hospitals and sanatoriums for the care of persons with mental and nervous illness. Twenty-eight sanatoriums in the central states are represented in the association, which has met each year at the same time and place as the Central Neuropsychiatric Association. A special meeting has been arranged to be held in Chicago on Jan. 25, 1935, at which papers on subjects dealing with the problems of private hospitals and related topics will be presented. The secretary of the association is Dr. D. A. Johnston, Box 4, College Hill, Cincinnati.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The twelfth annual meeting of the American Orthopsychiatric Association will be held at the Pennsylvania Hotel in New York, Feb. 21, 22 and 23, 1935. Dr. George S. Stevenson is the president. The office of the secretary is at 50 West Fiftieth Street, New York.

MONTREAL NEUROLOGICAL INSTITUTE

On Sept. 27, 1934, the doors of a new institute of neurology were formally opened in Montreal. The building is adjacent to the Royal Victoria Hospital, and the two institutions are connected by a bridge which forms one of the finest architectural features of a group of buildings, already impressive, high on the slopes of Mount Royal.

The new institute, built of Montreal stone, is owned by McGill University. Administration of the clinical activity in it is undertaken by the superintendent of the Royal Victoria Hospital as though it formed a part of that general hospital. Half of the building is devoted to laboratory investigation, the other half to the care of patients. Neurophysiologic, neuropathologic and biochemical laboratories are fully equipped on upper floors, and living quarters are provided for a limited number of research fellows. Consulting rooms are furnished for certain members of the attending staff.

Thirty-two public patients and fifteen private and semiprivate patients can be accommodated in the institute, while other patients may be cared for in the Royal Victoria Hospital. The clinical field is that of both neurology and neurosurgery, the director of the institute occupying the chair of neurology and neurosurgery at McGill University. French as well as English physicians have been appointed to the consulting staff, so that the institute is brought into direct association with most of the general hospitals in the city.

Half the cost of the construction of the building was defrayed by the Rockefeller Foundation and half by public-spirited citizens of Montreal. A donation of $1,000,000 was made by the Rockefeller Foundation, the annual income of which is to go toward neurologic research. The province of Quebec and the city of Montreal have undertaken to contribute to the upkeep of the public patients.

At the opening exercises, foundation lectures were delivered by Dr. Harvey Cushing and Dr. Gordon Holmes. The neurologists of Montreal have been trained largely in the English, American and French traditions, but it is anticipated that the opening of this institute marks the founding of a school of neurology peculiar to Canada.

Obituaries

SANTIAGO RAMÓN Y CAJAL
1852–1934

Santiago Ramón y Cajal died on Oct. 18, 1934, at the age of 82. Neurologists, anatomists and biologists in every land mourn his death, for they owe him a heavy debt of gratitude, although some who know his discoveries may not be aware who made them. For fifty years he contributed steadily to the field of neurohistology.

In Spain he stands for more than a histologist. He has been a symbol of the continuing virility of Spanish stock, a forecast of Spanish leadership in science and a leader in the renaissance of fine arts which is flooding Spanish life today. This movement is something more than a renaissance, for it includes science, which came into being while Spain still slumbered in the glow of her former glory. The romantic story of his life has been sketched in English several times,[1] and his own memoirs lay bare the romance which is described with great insight by Wilbur Sprong in this number of the ARCHIVES.

Ramón y Cajal never studied abroad. He was a spontaneous native product. After an indifferent medical training he began his brilliant career in histology equipped with one or two foreign books, a microscope and inspired curiosity. He was ever intense, working with fine frenzy day and night when the "scent was hot" and throwing himself into his avocations with a constructive insight which made him an authority on color photography, an artist of ability and a scholarly author of aphorisms and reflections.

Applause and fame came to Cajal but caused him little elation. He shunned public appearance, refusing to be Minister of Health. His daily routine took him no farther than laboratory and café. He carried out his own technical work, making his own drawings and accumulating a large library on histology. The Spanish government built a splendid institute on a hill in Madrid and named it the Instituto Cajal in his honor. But it came too late, in the twilight of his career. He found the ceilings too lofty and the rooms too grand and continued to work in a small laboratory in his own home.

A few years ago there was built in Madrid's park, the Retiro, along a pathway habitually followed by Don Santiago in his afternoon walk,

1. Penfield, W.: The Career of Ramón y Cajal, Arch. Neurol. & Psychiat. **16**:213 (Aug.) 1926. Garrison, F. H.: Ramón y Cajal, Bull. New York Acad. Med. **5**:483, 1929. Addison, W.: Ramón y Cajal: An Appreciation, Scient. Monthly, Aug., 1930, p. 178.

a monument to him. The monument includes an elaborate statue, in Grecian style, of the histologist looking down into a pool of water wherein he is supposed to discern the hidden meanings of biology. But according to the pupil who has been closest to Cajal during his later years, Señor de Castro, the master never entered the Retiro after the appearance of the monument, a characteristic reaction, for although somewhat jealous of his fame he invariably turned away from its ackunowledgment to a sequestered renewal of his efforts.

I saw Cajal last in his eightieth year, when I called on him in the company of his pupil, Señor del Rio Hortega. The old man had a cold, and we found him in bed sitting upright working on a manuscript, books piled beside the bed and ink spattered on the wall next to his impatient right hand. He was elaborating a final defense of the first child of his researches, the neuron doctrine. Deafness and feebleness, which had come on him recently, were shutting doors between him and the world, but his eyes blazed from under shaggy brows with unquenchable fire.

Now that the end has come, his life and achievement loom large in the history of neurology. He was a many-sided genius, impelled by that mysterious "whisper" that comes to God's chosen few, that draws them ever onward to explore beyond the horizons of existing knowledge, without rest and with no need for recompense other than to know that they have entered the promised land of discovery.

> God took care to hide that country till He judged His people ready.
> Then He chose me for His Whisper, and I've found It and It's yours.
>
> *(From Kipling's "Explorer")*

WILDER PENFIELD, M.D.

Abstracts from Current Literature

"Alcoholic" Polyneuritis: Dietary Deficiency as a Factor in Its Production. G. R. Minot, M. B. Strauss and S. Cobb, New England J. Med. **208:** 1244 (June 15) 1933.

Symptoms due to a deficiency of a nutritional factor may arise from the failure of the patient to ingest an adequate amount of that substance, but at least many weeks are required before symptoms clearly dependent on such a lack will develop in a healthy person. Partial dietary deficiency may result from a prolonged departure from an optimal diet without the development of symptoms distinctive of a particular syndrome. When this is the case, however, the occurrence of adverse factors, such as infection and intoxication, may precipitate disease states clearly recognized as produced by the lack of one or more nutritional factors.

Necessary material may not be properly elaborated because of a lack of gastro-intestinal secretions, such as occurs in pernicious anemia, or nutritious elements may be absorbed unsatisfactorily, leading to a state of deficiency exactly like that which develops if an insufficient amount of proper food has been ingested. The presence of gastric anacidity or states associated with it seems to be definitely a factor in enhancing the development of certain deficiency disorders.

The similarity of the symptoms and the pathologic process of multiple neuritis of beriberi due to a lack of vitamin B_1 and of alcoholic polyneuritis leads one to question whether these two conditions do not have a common etiologic basis comparable to the common basis of endemic pellagra and "alcoholic" pellagra. There are cases of polyneuritis resembling beriberi, of which we have seen several examples, in which a lack of absorption of vitamin B_1 can readily be attributed to a gross disorder of the small intestine, for example, chronic diarrhea following the removal of several feet of the small intestine. There has also been observed in Boston a group of patients with polyneuritis in the absence of alcoholism, infection or exposure to lead or other known poison, who had had a grossly abnormal diet for a long time, often associated with some defect of gastro-intestinal function. These patients improved relatively rapidly on eating appropriate food.

With these aspects of dietary deficiency and the relation of vitamin B_1 to multiple neuritis in mind, observations and views concerning "alcoholic" polyneuritis in relation to deficiency of dietary factors are presented. Fifty-seven patients with undoubted "alcoholic" polyneuritis who had gastric analyses performed or adequate dietary histories taken, and usually both, have been observed. In addition, the records of seventy-three additional patients without data concerning gastric secretions or dietary habits were examined. All of the patients had consumed alcohol, usually for many years, in excessive amounts, especially the type called "ardent spirits" or hard liquor.

It was possible to formulate the usual diet of forty-three patients. Only two had partaken of diets which could be considered adequate, if not optimal, for nutrition. The remaining forty-one patients had eaten little fresh food of any kind for at least many months and usually for several years, and they had almost always eaten sparsely of foods rich in protein. In many instances the diet had been deficient in calories as well as in protein, minerals and vitamins, so that a loss of from 20 to 40 pounds (9.1 to 18.1 Kg.) of body weight prior to admission to the hospital was common. When the caloric intake from food—not alcohol—was sufficient, it was chiefly derived from foods rich in carbohydrates.

Fractional gastric analyses were performed on forty-three patients. Only seven of the forty-three patients secreted normal amounts of hydrochloric acid in the gastric juice. It may be argued that this incidence of achlorhydria and hypochlorhydria is merely characteristic of chronic alcoholism, and this may be the case. Although many cases of chronic gastritis are ascribed to alcoholism and there may be deficiency in the secretion of free hydrochloric acid, we have been

unable to locate significant statistical data concerning the state of the gastric secretion in chronic alcoholism. It is evident that the patient with "alcoholic" polyneuritis abnormally frequently has achlorhydria, a condition which is associated perhaps with the development of certain deficiency states, such as pernicious anemia, pellagra and sprue, in which gastric anacidity is encountered respectively in about 99, 64 and 50 per cent of cases. Pellagra is associated with a lack of vitamin B_2, and some similar or associated factor may be involved in pernicious anemia and sprue.

Fourteen of the fifty-seven patients had dermatitis and other lesions characteristic of pellagra. There were other patients with chronic intestinal disturbances and minor cutaneous lesions that may have had a pellagrous origin. Several of our patients had edema that could be related to a deficiency of protein, although in only two were the plasma proteins determined. In both they were abnormally low. Edema associated with organic disease of the heart was present in at least six of the fifty-seven patients.

The characteristics of "alcoholic" polyneuritis are a predilection for the legs, intense pain, deep tenderness, hypesthesia of the skin and atrophy of the muscles with fibrous contractures. As in other forms of neuritis the onset is insidious; tremor, instability and muscular cramps are the precursors of foot drop or wrist drop; paresthesia and neuralgic pains precede the anesthesia, especially plantar hyperesthesia; loss of tendon reflexes can be observed when the motor weakness seems merely a muscular fatigability to the patient; muscular atrophy appears later; atrophy of the skin, cyanosis and edema are also late signs.

A description of the "dry form" of beriberi as seen in the Orient would be almost identical, word for word, with the foregoing description, although the severity of the process and wider distribution over the body are conspicuous.

Extracts from the literature on the pathologic process of alcoholism show how unsatisfactorily the field has been studied, but when viewed from a new standpoint of deficiency disease some order seems to rise out of the chaos. The pathologic process of alcoholism in one group of patients closely resembles that of beriberi, in which the lesions are essentially degenerative neuritis of the long peripheral nerves. Another group of patients, those with the Korsakoff syndrome, have a pathologic process much like that of pellagra, in which degeneration of the nerve cell in the cerebral cortex is the conspicuous lesion. A third, less well defined and perhaps more rare group have lesions of the spinal cord resembling those found in pernicious anemia. Scurvy has been mentioned by Nonne, and an analogy might be drawn between the vascular lesions of scurvy and those found in "polioencephalitis superior" due to chronic alcoholism.

Obviously the old narrow classifications must be broken down, for cases of disease due to dietary deficiency are known to present all these lesions, and clinically the classifications no longer can be dogmatic. For instance, "alcoholic pellagra" and "alcoholic beriberi" are becoming accepted diagnoses. It is not a question of fine differentiation of syndromes, but a problem of broad understanding of the pathologic process, which is alike in all but variously localized. This localization of the process in different parts of the nervous system causes different symptoms. In other words, the imbibing of alcohol may, by its effect on the digestive tract and the diet, precipitate neuronal degeneration (and perhaps vascular lesions) in the brain, the spinal cord or the peripheral nerves. If the process is largely in the brain and peripheral nerves, Korsakoff's syndrome results. If the brain is affected severely with less degeneration of the cord and least in the peripheral nerves, the syndrome is that of pellagra. The converse of this picture is "alcoholic" polyneuritis, with Nonne's "myelitis intrafunicularis" intermediate between the two.

Forty of the fifty-seven patients have been treated by a diet rich in complete proteins, minerals and vitamins. This daily diet has included from 150 to 250 Gm. of beef liver pulp, 200 Gm. of orange juice, 100 Gm. of muscle meat, 500 cc. of milk and large helpings of fresh vegetables, fruits and butter. Food consisting of concentrated carbohydrates have been given sparingly. Daily about 60 cc. of

cod liver oil and about 12 Gm. of autolyzed yeast or extractives have been given each patient, and, when indicated, iron has been given. It is our distinct impression that under this regimen recovery has been observed more uniformly and with greater rapidity than previously.

From observations of fifty-seven patients and a study of the records of seventy-three additional patients, together with a survey of the literature, it appears that dietary deficiency, probably especially the lack of vitamin B_1, plays an important rôle in the production of "alcoholic" polyneuritis. The deficiency can be attributed not only to inadequate intake but to the state of the gastro-intestinal tract and the presence of factors that can inhibit the effectiveness of nutritional elements.

AUTHORS' ABSTRACT.

INTERRELATIONS BETWEEN PSYCHOANALYSIS AND THE EXPERIMENTAL WORK OF PAVLOV. THOMAS M. FRENCH, Am. J. Psychiat. **12**:1165 (May) 1933.

The technic of Pavlov and that of Freud appear to be diametrically opposed; the former is a synthetic method, working from simple responses to ultimately complex behavior reactions; the latter is an analytic approach, starting from complex human behavior and seeking an explanation in terms of simple units of trend. They differ in subject matter as well as in method; the freudian concerns himself largely with internal stimuli—wishes and drives; the disciple of Pavlov, with simple external agencies. Yet there are more similarities than the casual student might anticipate, and there are many parallelisms. Just as a motor response may be brought about by an oblique stimulus with which it had once been associated, a psychic response may be precipitated by a stimulus not apparently directly associated with it. The repression of a complex (such as the Oedipus in women) following repeated failure of the desire to be gratified is compared to the experimental extinction of a conditioned reflex by withholding the usual associated stimulus. The fact that the extinguished reflex will reappear under favorable conditions, or even spontaneously, is evidence that it must have persisted at some deeper level—analogous to the subconscious existence and subsequent reevidencing of a repressed complex. The "positive induction" of the behaviorist is compared to such phenomena as "displacement upward" of the analyst. Differentiation of response, whereby an animal is trained to respond only to a specific stimulus when at first it responds to a variety of stimuli of the same general type, is not unlike sublimation, in which only the socially acceptable form of a previously undifferentiated tendency is retained. The process of learning, whereby sterile stimuli are ignored, is essentially like the adjustment to reality of the freudians. The confusion of excitatory and inhibitory response to mixed stimuli in the untrained animal is compared with the elements of conflict in the human being. French calls attention to the fact that conditioning cannot take place if prepotent reflexes already exist which are strong enough to prevent response to neutral stimuli. In analytic terms, the same phenomenon may be expressed as the necessity for free psychic energy before the ego can adjust to external reality. Nor can objection be raised that the phenomena are so different that analogies are impossible. For the apparently simple mechanisms described by Pavlov are not so simple as they seem. For example, the salivary reflexes are only isolated elements in a complex goal-directed activity toward the satisfaction of hunger drives. Even such apparently unphysiologic problems as that of the dream can be fitted into the pattern of reflexologic investigation. A hungry man dreams of food; in the man's previous experience the sight of food has been followed by gratification; the state of hunger has, as it were, become conditioned to elicit some sort of reproduction of a previously satisfying experience. The so-called "paradoxical phenomena" of Pavlov (in which a weak stimulus produces a disproportionately strong response) is compared to the representation of an unconscious psychic element by its opposite, or perhaps to displacement of psychic emphasis. The therapeutic service of psychoanalysis is described as making a traumatic experience accessible to the learning process.

French proceeds step by step to draw parallels between the phenomena and the terminology of psychoanalysis and the experimental observations and language of the disciples of Pavlov. The paper is lengthy (40 pages) and should be read in full for an adequate understanding of French's approach.

DAVIDSON, Newark, N. J.

STERILIZATION, Editorial, Brit. M. J. **1**:156 (Jan. 27) 1934.

This editorial reviews the report of a committee of eight appointed by the Board of Control to study the question of sterilization of the unfit. The committee's first task, admittedly impossible within the limits of its report, was "to examine and report on the information already available regarding hereditary transmission and other causes of mental disorder and deficiency." The committee states that the witnesses who gave evidence were not in agreement as to the mode of transmission of mental defect and disorder, though all recognized heredity as an important factor in the causation of these conditions. A substantial, if not high, proportion of patients in hospitals and institutions for the mentally defective have one, two or more relatives who have suffered from some form of mental disease or defect. Thus, hereditary factors were found or inferred in 91 per cent of the cases considered and environmental factors in 71 per cent.

The committee was asked to consider the value of sterilization as a preventive measure, having regard to its physical, psychologic and social effects and to the experience with legislation permitting it in other countries. That it will serve as a substitute for the provision of institutional accommodation is illusory. The impossibility of procreation will not save such persons from being a social menace. The case for sterilization as a social measure hinges virtually on two points: (1) that approximately two thirds of all defective persons are capable of community life and (2) that defectives make inefficient parents. The committee recognizes that some defective persons are able to run a household with a fair measure of success and wish to marry, and if sterilized could marry without ill effect. As against this, there is the risk of sexual promiscuity, which the committee, though it has failed to find any evidence of this after painstaking inquiring, does not dismiss as imaginary.

The committee came to the conclusion that in the present state of knowledge the case for compulsory sterilization cannot be established. The committee assumes that the legislature would not feel justified in telling any person to submit to sterilization unless it could be shown beyond reasonable doubt that at least some of the offspring either would be mentally defective or would have a mental disorder, and of this no proof can be produced. The committee unanimously recommends that voluntary sterilization be sanctioned. The committee argues forcibly that the case for legalizing sterilization rests on the broad principle that no person, unless conscience bids, should be forced to choose between complete abstinence from sexual activity or risking bringing into the world children whose disabilities will make them a burden to themselves and to society.

Legalization of sterilization affects the carriers of grave physical disabilities that are shown to be transmissible. Unfortunately the carriers of mental disabilities, though estimated as ten times more numerous than the affected persons themselves, cannot be identified with the same certainty as can the carriers of, say, hemophilia or hereditary blindness, the mode of transmission of which is known.

FERGUSON, Niagara Falls, N. Y.

ETIOLOGY OF CHRONIC ALCOHOLISM. JOHN L. SMALLDON, Psychiat. Quart. **7**:640 (Oct.) 1933.

An investigation of hospitalized patients with alcoholism suggests to the author that much support may be found for Freud's theory of a psychogenic chronic alcoholism. Homosexuality and other repressed sexual forces may frequently be found. Many character traits of the inebriate may be explained as the result of

partial oral fixations or instances of oral sadism. The repeated urgency of alcoholic desire is attributed to the erogenous nature of the mouth. An alcoholic spree removes the resistance to an open expression of homosexuality; it dissipates, for example, the usual aversion to tenderness between men, and permits men to embrace one another and to weep, cry and play together. Based on the sense of heterosexual inferiority, the inebriate indulges in boastful fantasies of heterosexual prowess. The delusion of marital infidelity may readily be explained as a projection of this mechanism. Two illustrative cases are cited.

A man, aged 39, who had a great fondness for his mother, gave a history of running away from home in childhood because of antagonism to his father. He married a girl who is described as closely resembling his mother. He indulged in an extensive spree following the shock of his mother's death and shortly thereafter deserted his wife and went to keep house for his father. Women did not have a place during his alcoholic debauches, which were usually prolonged and conducted exclusively in masculine society. During the sprees he occasionally talked about his mother and had hallucinatory experiences concerning his contact with her. At the hospital he suffered from an attack of delirium tremens, during which he saw his old friends (masculine) threatening to kill him with machine guns. In one hallucinatory experience a man threatened to cut his throat with a knife 8 inches (20 cm.) long. The one person in the ward who was most successful in pacifying him was a female nurse. In commenting on this case, Smalldon stresses the phallic symbols (machine guns and knife), the fear of men (visions of his male friends manning the threatening guns, fear of his father), the influence of women (excessive mother love, the resemblance between wife and mother, the influence of the nurse) and the womanless nature of the orgies. The patient's position as cook and housekeeper for his father is also emphasized.

In the second case, the patient had a strong mother attachment, marital difficulties, hallucinations of a bearded man threatening him with a knife, dislike of working with women, auditory hallucinations of being called homosexual and an overattachment to a sister.

Smalldon finds this freudian hypothesis more acceptable than any other single explanation for chronic alcoholism. An explanation on a conscious level, in any event, must be rejected, because of the inadequacy of conscious motives and conscious wishes in correcting the desire for alcohol. DAVIDSON, Newark, N. J.

THE AUTONEURO-ENDOTOXIN. O. MECO, Riv. di pat. nerv. **41**:439 (March-April) 1933.

The author has studied the neurolytic power of cerebrospinal fluid by adding pieces of fresh guinea-pig brain to test tubes containing fluid. He has compared the disintegration of the brain tissue in normal cerebrospinal fluid and in physiologic solution of sodium chloride used as a control. After the brain substance has been entirely disintegrated in cerebrospinal fluid, the same spinal fluid is used to test for enhanced neurolytic power resulting from the dissolved products of disintegration of the brain tissue. The conclusions are: 1. Disintegration of cerebral tissue produces a substance, as yet undefined, possessing neurolytic power; this substance is ultrafiltrable. 2. This ultrafiltrable substance originates in all probability from disintegration of gray matter, the products of disintegration of gray matter having disclosed a much higher neurolytic power than those of the white substance. The author thinks that the neurolytic substances may be derived from nerve cells. 3. Products of disintegration of nerve tissue possessing strong neurolytic power are unable to disintegrate other types of tissues. It may therefore be inferred that the neurolytic property is specific; it may be added that the neurolytic substance acts with greater activity on nerve cells than on nerve fibers. 4. The products of disintegration of nerve tissues are apt to produce neurolysis in simple physiologic solutions, though the presence of cerebrospinal fluid enhances this power. 5. In general, the neurolytic power is proportional to the degree of damage of the nerve tissue itself. Pathologic processes of nerve tissue, particularly toxic

ones and postmortem changes, render nerve tissue more easily attacked by neurolytic agents of the cerebrospinal fluid. In turn, pathologic processes bestow on the tissue itself a stronger neurolytic power. 6. Having established experimentally on living animals that the processes of disintegration of nerve tissue are apt to create a severe pathologic condition and establish lesions in the brain comparable in all probability to those found in vitro on fragments of the nervous tissue immersed in cerebrospinal fluid, it may be stated that the substances endowed with neurolytic power may also act on the nervous system during life. 7. Because the neurolytic substance is a normal and vital product of the physiologic or pathologic activity of nerve cells, because it has a definite and specific action on nerve tissue, because it is a product of nerve cells and because it is a toxic product apt to damage and disintegrate nerve tissue, it may be called "autoneuro-endotoxin."

FERRARO, New York.

CEREBRAL BIRTH CONDITIONS WITH SPECIAL REFERENCE TO THE FACTOR OF HEMORRHAGE. CLARENCE A. PATTEN and BERNARD J. ALPERS, Am. J. Psychiat. **12**:751 (Jan.) 1933.

Patten and Alpers analyze the pathologic changes in thirty infant brains. Seventeen showed subarachnoid hemorrhage, and twenty-six exhibited subependymal bleeding. Analysis of the facts concerning the deliveries failed to indicate any specific factor—such as duration of labor, use of anesthetics or instruments or type of presentation—as being responsible for the abnormality. Scattered throughout the brains were petechial hemorrhages, concentrated chiefly in the subependymal regions around the lateral ventricles. Many lay within the germinal foci of neuroblasts and spongioblasts surrounding the ventricles. Involvement of the white substance under the cortex was relatively infrequent.

Earlier studies have focused attention on the importance of subarachnoid hemorrhage in birth injury. Patten and Alpers, however, are inclined to minimize its importance. They point out that large subarachnoid extravasations are followed quickly by death and that less abundant bleeding is generally followed by absorption. They cannot explain the cortical changes commonly associated with birth in this manner. Subependymal bleeding, on the other hand, seems to them of graver significance. This area is vital to future development of the brain because of the growth of the glial elements here. Their study shows that the oligodendroglia cells—important for myelinization—are affected greatly by subependymal hemorrhage. Extravasations of blood in this area destroy the spongioblasts from which the oligodendroglia cells are derived, thus interfering with the capacity of the brain to form myelin. The authors recall the work of Flechsig demonstrating that myelinization occurs in sensory nerve fibers long before it does in the cortical motor tracts. Sensory structures are nearly, if not fully, myelinated before birth. On the other hand, only the motor fibers that are essential to life (breathing, sucking, swallowing etc.) are myelinated early, while those concerned with voluntary movements and those from the forebrain receive their sheaths from above downward more slowly and at a later date. This, combined with the observations on subependymal hemorrhage, offers an explanation for the almost exclusive predominance of motor defects in cerebral palsies at birth and for the intellectual defects which frequently accompany them.

DAVIDSON, Newark, N. J.

VENTRICULOGRAPHY AND ENCEPHALOGRAPHY BY MEANS OF THORIUM DIOXIDE SOLUTION. H. H. SCHOENFELD and WALTER FREEMAN, M. Ann. District of Columbia **2**:277 (Dec.) 1933.

In this brief article and exposition of cases, Schoenfeld and Freeman report the results of intraventricular injection of thorium dioxide. They believe that this is the first time the procedure has been carried out on human beings. They realize that animal experimentation has not been entirely satisfactory but believe that

at least a part of the ill effects reported were due to faulty technic. Certain advantages of thorium dioxide, particularly its miscibility and the resulting clearer definition of dependent portions of the ventricular system, outweigh the possible disadvantages. The authors used this procedure in clinical cases.

Case 1 was that of a white man, aged 29, who for two months had had symptoms suggestive of an intracranial neoplasm. A ventricular tap was done with some difficulty, the impression being that the ventricles were small or distorted. It was feared that injection of air under these circumstances would be unsatisfactory. Accordingly, 5 cc. of thorium dioxide was drawn into a syringe and thoroughly mixed with cerebrospinal fluid from the ventricle. The total quantity was injected into the ventricle, and roentgenograms were taken. Excellent pictures of the ventricles resulted. Roentgenograms taken after twenty-four hours showed no residual thorium dioxide. A left homonymous hemianopia appeared on the day after operation, but disappeared promptly. The patient was discharged on the sixth day with no apparent ill effects from the injection.

Case 2 was that of a Negro, aged 63. The ventricles were apparently encountered at a very shallow depth, and thorium dioxide mixed with cerebrospinal fluid was injected. The roentgenograms showed thorium dioxide spread over the whole occipital subarachnoid space, evidently as a result of the fenestra of the needle not having entered the ventricle. There was no unusual reaction; the patient left the hospital in a few days in an improved condition.

In view of the absence of serious reaction following direct injection of thorium dioxide into the ventricles, it is thought that the method, because of its possible advantages, deserves the test of further clinical investigation.

SCHNEIDER, Washington, D. C.

NEUROMATOSIS OF THE VERMIFORM APPENDIX. KIYOSKI HOSOI, Arch. Path. **16**:500 (Oct.) 1933.

In 1921, Masson and Maresch reported the occurrence of neuromatous tumors in obliterated appendixes. At that time they believed that these growths were of the nature of amputation neuromas, caused by a division of the sympathetic filaments of the mucosa by an ulcerative process or by injury to the nerves by an inflammatory process. Masson recently stressed the close interrelationship between neuroma and chromo-argentaffin or carcinoid cells. He showed that appendicular neuromas arise from the nerves of the periglandular plexus and that they regress individually.

Of 344 vermiform appendixes removed consecutively at operation and showing no evidence of acute inflammation, 165, or 48 per cent, had a distally or totally obliterated lumen and 195, or 56.7 per cent, showed neuromatosis. Of the 195 cases of neuromatous growths, 135, or 69.2 per cent, occurred in obliterated appendixes and 60 cases, or 30.8 per cent, in nonobliterated ones. This gave an incidence of 82 per cent of neuromatous appendixes for all obliterated appendixes.

There was nothing characteristic grossly to indicate the presence of neuromatoses of the appendix. When the neuromatous growth was grossly noticeable, its cut surface appeared opaquely grayish white, usually without well demarcated borders. The larger growths in this series measured not more than from 1.5 to 2 mm. in diameter. The number of neuromatous growths varied from one to many. When multiple, they were linked together by many nerve fiber strands. They appeared as loosely anastomosing strands of nonmedullated nerve fibers or as islands of compact interlacing bundles of spindle-shaped cells, always located centrad to the muscularis mucosae. If the neuromatous tumor mass was large enough, the muscularis mucosae was closely apposed to it along the periphery in the manner of a capsule. The tumor mass rarely broke through the muscularis mucosae. These neuromatous growths contained a variable admixture of either argentaffin cells or lymphocytes. The Masson trichrome stain should be employed before an appendix is discarded as being negative for neuromatosis.

WINKELMAN, Philadelphia.

A Study of Postural Persistence in Cases of Postencephalitis. Lowell S. Selling, J. Nerv. & Ment. Dis. **78**:24 (July) 1933.

Selling makes use of the phenomenon described by Hoff and Schilder on postural persistence. When both arms are raised horizontally, with palms down, the left arm then depressed at an angle of 45 degrees and both arms later raised to the horizontal, the patient being blindfolded meanwhile, the arm previously depressed is found still to be below the other arm and the true horizontal. Hoff and Schilder found this phenomenon absent in six cases of definite postencephalitic parkinsonism.

Selling discovered that for clinical purposes the best results in the test are obtained when the posture is maintained for at least twenty seconds. Prolongation of posture beyond that time results in a diminution of the phenomenon. No sexual differences were observed, but the phenomenon was more marked in the hand less often used for skilled operations. The upper quadrant postures were found to result in greater deviation than the lower, but the latter were more convenient for testing. Among fifty normal persons the deviation ranged from 3 to 7 cm. The phenomenon being an unconscious one, no matter how hard the subject tries to approximate the horizontal with both hands he is likely to be unable to do so.

Thirty-two cases in which some degree of parkinsonism was present showed diminished deviation of less than 3 cm. In more than half the trials there was no deviation. In two cases in which the parkinsonism was unilateral, the phenomenon of postural persistence was not demonstrated on the involved side, while it approached the normal on the unaffected side. The fact that postural persistence is so definitely lost in extrapyramidal disease makes it thus a corroborative symptom of parkinsonism.

Hart, Greenwich, Conn.

New Conception of Dioptric Power. Joseph I. Pascal, Arch. Ophth. **9**:244 (Feb.) 1933.

Students of physiologic optics have noted certain apparent discrepancies in the calculation of dioptric powers as given by different authorities. The reasons for these variations are discussed in fair detail. The dioptric power of a refracting surface or of any system as a whole may be expressed as the reciprocal value either of the first (actual) or of the second (actual) focal length. As these two are different except when the first and last mediums have the same index, two different expressions are obtained for the power of the surface. Usually the power as determined by the first (actual) focal length has been used as the standard. This method of denoting dioptric power has been the prevalent method and is the only one used in practically all English works on the subject. A new and better method of denoting dioptric power has recently been introduced, especially by continental writers. This method involves the conception of a "reduced" focal length.

By a simple mathematical relation, the two (actual) focal lengths can be resolved into a single value, the so-called reduced focal length, and the reciprocal of this value stands for the refracting power of the surface or the system. From the "reduced" focal length the two (actual) focal lengths can be easily obtained by multiplying the reduced focal length by the corresponding index, i. e., by the first index to obtain the first focal length and by the second (or last) index to obtain the second focal length. A single formula (D equals aM) is presented and explained. It suffices for all calculations and is especially easy of application when this method of determining dioptric power is being used. The paper is essentially mathematical, as is all physiologic optics, but it has been made so clear that most readers can appreciate the author's desire to eliminate some of the discrepancies mentioned.

Spaeth, Philadelphia.

Clinical Perimetry. P. Halbron, Ann. d'ocul. **170**:817 (Oct.) 1933.

Undoubtedly the simplest method of practicing perimetry is for the examiner to use his hands as test objects and while facing the patient compare the visual

fields. However, this method is inaccurate and should be used only in rare cases, when the visual fields cannot be studied by any other method. Ferree and Rand have tried to make practical the use of colored test objects by reducing the normal variations of the chromatic visual fields to a minimum. Groenouw, Bjerrum and others prefer to increase the sensitiveness of perimetry by using a white test object, with which they claim to obtain more reliable results. Finally, Halbron describes a recently constructed apparatus designed on new principles, different from the classic perimeters.

Quantitative perimetry should be practiced with exactness and understanding. A gray perimeter with proper lighting and equipped with a good system of fixation is the best. The test objects and the method of perimetry are not the same for delimiting the peripheral limits of the visual field and for exploring the paracentral region. For the periphery, white test objects of 3 mm. are used. They are carried the length of the meridians from the periphery, toward the point of fixation. For the paracentral region, a white test object of 1.5 mm. is moved about the point of fixation after mapping the blind spot of Mariotte. The field for red may also be tested.

Perimetry, thus practiced, is an easy method for the practitioner. Halbron realizes that he does not obtain the exact scientific precision of Ferree and Rand, but in a subjective examination absolute accuracy is unnecessary. With his technic he has obtained results in studying the visual field that are comparable to those of Ferree and Rand. He advocates a sensible and rapid method which is an improvement on the ones previously used.

BERENS, New York.

A CLINICAL CONSIDERATION OF MENTAL DEFICIENCY. HOWARD W. POTTER, Psychiat. Quart. **7**:195 (April) 1933.

Potter suggests that mental deficiency is not a clinical entity but a symptom; to classify feebleminded persons on the basis of the intelligence quotient is as logical as classifying fevers on the basis of the temperature reading. The training of the retarded patient, furthermore, should be based on the underlying clinical condition and not on the mental age. In many instances, feeblemindedness may be considered to be due to a structural defect in the brain tissue, but more often it is caused by an inefficiency of cerebral function. In cases of the latter type, the outlook is better, for when there is a disorder in function there is hope of improved function by retraining. Potter suggests the wider use of the clinical classification recommended by the Committee on Nomenclature of the Association for the Study of the Feebleminded. In this classification, mental deficiencies are placed in seven broad clinical groups: (1) prenatal, (2) infectious, (3) traumatic, (4) convulsive, (5) metabolic, (6) neoplastic and (7) idiopathic. The author stresses the importance of considering feeblemindedness from the social as well as from the clinical and psychologic aspects. For example, a child with juvenile dementia paralytica is clinically syphilitic; socially, he is an idiot or an imbecile. To designate the condition, however, as "mental deficiency" with a certain intelligence quotient is to classify it improperly. Treatment and training will be more effective when the social and medical (clinical) conditions are taken into consideration. In the present methods of training excessive stress is laid on the mental age and the intelligence quotient.

DAVIDSON, Newark, N. J.

RESULTS OF SURGERY IN SPINA BIFIDA. ANATOLE KOLODNY, J. A. M. A. **101**:1626 (Nov. 18) 1933.

On the basis of a study of seventy-nine cases of spina bifida, Kolodny concludes that surgical repair is the only treatment of spina bifida. If not operated on, the majority of the children die within the first year of life. The best time for operation varies according to the condition of the skin covering the defect: if there is no break in the skin of the sac, it is best to wait until the weight lost by the child after birth is regained; if there is an ulceration of the skin,

with or without free drainage of cerebrospinal fluid, one should wait until the draining sinus is healed; however, if complete rupture of the sac is imminent, operation should be done forthwith. A broad base of the spina bifida and a wide defect in the vertebral arches are not contraindications to operation. Paralysis is not a contraindication to surgical treatment; after the spinal cord and the nerve roots are freed the child may regain considerable function in the lower extremities and in the sphincters. The importance of the absorptive power of the dural sac of the spina bifida for the prevention of a hydrocephalus is overestimated; in cases in which a hydrocephalus has ultimately developed, either it was evident prior to the operation or it developed in the wake of a postoperative infection. The operative mortality in spina bifida is greatly reduced as a result of (1) a prevention of loss of body heat during the operation, (2) a prevention of loss of blood, (3) a prevention of rapid loss of spinal fluid, (4) the use of a brief and light anesthesia and (5) the return of the infant to the preoperative routine of feeding immediately after the operation.

EDITOR'S ABSTRACT.

MYASTHENIA GRAVIS: FOURTH REPORT: ONSET AND COURSE OF DISEASE. W. M. BOOTHBY, J. A. M. A. **102**:259 (Jan. 27) 1934.

Between April, 1932, and June 10, 1933, Boothby observed twenty cases of myasthenia gravis. He presents a table giving the duration of the symptoms before the diagnosis was made and the total duration of the disease up to June, 1933, as well as the order in which the symptoms of the disease developed. In seven of the twenty cases there was a history of an acute infection shortly before the onset of the symptoms of myasthenia gravis. The order of the onset of symptoms is, with minor variation, consistent and characteristic. The course of the disease is usually gradual, with involvement first of one group of muscles and then of another, with irregular periods of remission or intermission. On the other hand, some patients present a fulminating type of the disease, with rapid and progressive involvement of various groups of muscles, which within four or five weeks after the onset of the disease may end in death from profound weakness, inanition and dehydration unless proper steps are taken in time to prevent these complications. The author carried out an extensive investigation of the chemistry of the urine and blood in all of his patients. The blood shows no characteristic or consistent change in either the nitrogenous or the inorganic constituents, which is of value in the diagnosis of the disease. The urine shows no abnormal constituent other than creatine. Unfortunately, laboratory data are of little practical help in arriving at the correct diagnosis, although the course of excretion of creatine is of considerable value in following the progress of treatment. Both ephedrine and glycine are valuable drugs in the treatment of the disease, and by their proper use a large proportion of patients with myasthenia gravis are benefited; many are so greatly helped that they can continue to work.

EDITOR'S ABSTRACT.

LYMPHOGRANULOMATOSIS MALIGNA (HODGKIN'S DISEASE), WITH INVASION OF THE SPINAL CANAL AND PARAPLEGIA. M. J. COOPER, J. A. M. A. **102**:917 (March 24) 1934.

Cooper discusses the clinical and neuropathologic features in a case of lymphogranulomatosis with an attempt to correlate, as far as possible, the clinical picture in this and previously reported similar cases with the gross and microscopic pathologic changes. In this case there was a direct extension of lymphogranulomatous tissue from an extradural tumor through the nerve roots, particularly through their fibrous septums, to the subdural space. There is apparently a greater affinity of this type of abnormal tissue for the structures comprising the lymphatic system, in preference to the structures of the nervous system. The vascular congestion was presumably secondary to compression or occlusion of the vessels in their courses along the nerve roots, and the pronounced degenerative changes in

the substance of the spinal cord have been attributed to this factor. On the basis of the changes found in this case and those in similar cases reported by other observers, it is concluded that (1) the nerve roots afford a route by which lymphogranulomatous tissue may reach the subdural space, probably through the lymphatic spaces of the roots rather than by the substance of the nerve fibers; (2) the spinal dura mater is relatively more resistant to penetration than are the septums of the nerve roots; (3) paraplegic symptoms may result not only from direct compression of the spinal cord but from obstruction to the circulation of the cord as a result of compression or invasion of the vessels accompanying the nerve roots.

EDITOR'S ABSTRACT.

OBSERVATIONS UPON THE FORM AND NATURE OF THE "GRASPING" MOVEMENTS AND "TONIC INNERVATION" SEEN IN CERTAIN CASES OF LESIONS OF THE FRONTAL LOBE. F. M. R. WALSHE and E. GRAEME ROBERTSON, Brain **56**:40 (March) 1933.

The disharmony of the recorded facts and theories concerning "grasping" and tonic innervation is reviewed. In the eight clinical cases presented there was evidence of a lesion involving the frontal lobe and in all but one there were also signs of an associated lesion of the pyramidal tract. All the patients showed unequivocal signs of impairment of psychic function. The stages of evolution and dissolution of these phenomena are discussed: (1) the grade of evolution in patients who show little psychic reduction; (2) the grade of full development in patients whose mental state is such as to permit visual fixation and some degree of attention; (3) the first grade of dissolution of the grasping phenomena in completely apathetic or mildly stuporous patients, and (4) the final grade of dissolution in patients who are semiconscious and cannot be roused to attention. There are phenomena of two distinct orders: (1) a grasping movement of the fingers, which is highly coordinated and reveals the activity of the cerebral cortex, and (2) a tonic contraction of muscles elicited solely by stretching, which resembles other known tonic reflexes and is involuntary. It is suggested that the region of the cortical origin of the frontopontile path is involved. The authors believe that the volitional component should be called "grasping movements," since these movements are neither reflex nor "flexed." For the reflex component, "tonic innervation" remains the most suitable term.

MICHAELS, Boston.

MORPHOLOGY AND CHARACTER. E. LANDAU, Charact. & Personal. **1**:238 (March) 1933.

Reviewing the history of attempts to discover the psychic aptitudes of a person from an analysis of his outward form or his internal anatomy, Landau is impressed by the relatively static nature of all previous researches. The physiognomy of Lavater and the phrenology of Gall have proved equally sterile, the former relying on the fixed configuration of the face, the latter on the changeless form of the skull. The classifications of Sigaud and Kretschmer have proved useful but of limited application, and represent conclusions drawn from fixed characteristics: body morphology. Nor have the researches of Lombroso, Poynter and Strida revealed any conclusive data as to a relationship between the form of the human cerebrum and the psychic constitution of the subject. Recent studies of the cyto-architecture of the cortex have failed to provide any anatomic or histologic basis for character changes; indeed von Economo, in his investigation of the pathology of encephalitis, has in some degree dethroned the cortex by discovering or at least hypothecating that the basal ganglia may regulate will, initiative and affect. It becomes clear, therefore, that simple anatomic investigation is proving futile in a search for a determinant of personality. It is in the relatively unexplored field of neurophysiology and biochemistry that hopes now lie; research into dynamic rather than static properties of the person, with the widening of the horizon of knowledge of the hormones, the sympathetic nervous system, the endocrine glands and the chemical and neurophysiologic changes within the body offers most promise.

DAVIDSON, Newark, N. J.

CRIMINALITY AND DELINQUENCY IN TWINS. AARON J. ROSANOFF, LEVA M. HANDY and ISABEL A. ROSANOFF, J. Crim. Law & Criminol. **24**:923 (Jan.-Feb.) 1934.

Records were taken from 1,008 pairs of twins of whom one or both was affected by mental disorder and from 313 pairs of normal twins. From these a study has been made of criminality, juvenile delinquency and behavior difficulties, which shows that causative factors of mental and behavior difficulties are pregerminal, germinal, embryonic, fetal, natal or postnatal, and that they may be simple, multiple (or variable) or complex. Comparisons are made with the studies of Johannes Lange in Germany and of Legras in Holland. The findings show that criminality is significantly more common in the male than in the female sex, though this contrast is less marked in the group showing juvenile delinquency and almost nonexistent in the group with behavior difficulties in childhood. Monozygotic twins are more closely alike than are any other two persons who could be selected, but "identical twins" are nonexistent. Injury to the head may produce a change in a person's character that may establish persistent criminal tendencies which previously did not exist. This study indicates that in two thirds of the cases of adult criminality in monozygotic twins, if one is criminal both are criminal In the remaining one third of the cases, in which only one of each pair of twins is criminal, five possible explanations for the development of the criminal tendencies are cited. In the juvenile delinquency group, of 16 pairs of male dizygotic twins, only one is affected in 5 instances and of 9 pairs of female dizygotic twins, both were affected in all cases.

SELLING, Detroit, Mich.

NATURE OF SKIN REACTIONS PRODUCED BY HEAT-INACTIVATED POLIOMYELITIS VIRUS. ALBERT B. SABIN, WILLIAM H. PARK and CLAUS W. JUNGEBLUT, Arch. Int. Med. **51**:878 (June) 1933.

Inoculation experiments were conducted to determine whether persons recovered from or otherwise resistant to poliomyelitis possessed any cutaneous allergy to the heat-inactivated virus. It is known that monkeys convalescing from experimental poliomyelitis show a febrile reaction to subcutaneous injection of the virus. The preparation used in the experiments of Sabin, Park and Jungeblut was made from spinal cords of monkeys with experimental poliomyelitis, while similar extracts from normal monkeys were used as controls. The technic for preserving and extracting the virus is described. The dose used was 0.2 cc., injected intracutaneously into the forearms. Only responses showing edematous, erythematous vesicles of more than 100 sq. mm. were recorded as positive. In a group of thirteen children convalescing from poliomyelitis, only four showed a positive response to the serum of the poliomyelitic cord, while among twelve normal children (without a history of poliomyelitis), the same number (four) showed a definite reaction. None of the twenty-five responded positively to extract from a normal monkey cord. Among twenty convalescing adults, twelve exhibited a positive response to the serum of the poliomyelitic cord and ten to extract of the normal monkey cord. Among seventeen normal adults, nine had a positive reaction to the virus-containing preparation, and eight to the extract of the cord of normal monkeys. From this it would appear that there is no definite evidence now available for the cutaneous allergy to poliomyelitis in human beings.

DAVIDSON, Newark, N. J.

EXPERIMENTAL CONVULSIVE SEIZURES. S. BERNARD WORTIS, J. Nerv. & Ment. Dis. **77**:233 (March) 1933.

Wortis employed intravenous injections of an alcoholic solution of camphor monobromide in cats and found that from 0.018 to 0.026 cc. per pound of body weight produced a generalized fit. Rapid myoclonic convulsive discharge in different parts of the body, with pupillary dilatation, was followed by a generalized clonic convulsive seizure with loss of sphincter control and loss of consciousness.

Experiments were made with cats in which various portions of the brain had been injured or removed, such as the frontal cortex, motor cortex, cerebellar cortex, parieto-occipital lobe, corpus striatum, tuber cinereum, corpus callosum and spinal cord. Some animals were subjected to trauma of the brain, and some to suprarenalectomy and to thyroidectomy. Extradural bodies were placed inside the skull to cause pressure against various parts. Finally, the effects of certain drugs, such as ether, chloroform, caffeine, epinephrine, ergotoxine, nicotine and bromides, are discussed. From a survey of past and current theories and experimental work on convulsions the author concludes that vasoconstriction of cerebral vessels during some generalized fits cannot be denied, but that this is always the cause of generalized convulsive seizures may well be disputed. He thinks it more logical that during convulsive seizure there is a discharge of stimuli which flow out through available neural pathways, those in the cerebrospinal system resulting in motor phenomena, and those in the vegetative nervous pathway producing characteristic sympathetic reactions, such as salivation, sweating and blanching. Vasoconstriction of cerebral vessels is certainly not the only mechanism causing the seizures.

HART, Greenwich, Conn.

NEOPLASM OF THE CHOROID PLEXUS. GAYLORD W. GRAVES and MAURICE M. FLIESS, Am. J. Dis. Child. **47**:96 (Jan.) 1934.

The authors call attention to the fact that neoplasms of the brain in infancy occur more frequently than one would expect from the frequency of reports of such lesions. Some of the general symptoms of increased intracranial pressure are seen in other conditions in infancy. The authors were able to find in the literature only one other report of a neoplasm of the choroid plexus in so young a subject. This type of tumor is rare at any age. The symptoms which their subject presented were nonprojectile vomiting, obstinate constipation and loss of weight. Various feeding formulas had no effect on the vomiting. At first the child was asthenic, listless and dehydrated; the anterior fontanel was depressed and no symptoms referable to the central nervous system were found. After dietary treatment for six days the patient became more apathetic and stuporous. There were inconstant deviation of the eyes to the left, upward and inconstant horizontal nystagmus, sluggish pupillary reactions to light and in accommodation and early papilledema. Spinal tap showed xanthochromic fluid which was under no increased pressure, formed no pellicle and was bacteriologically sterile. Ventricular punctures revealed xanthochromic fluid under increased pressure. The age of onset was 8 months; the duration of the illness was six weeks. From the standpoint of differential diagnosis, the authors suggest that in the case of any infant who vomits persistently and in whom abdominal disturbances may be excluded a potential diagnosis of meningitis, tumor of the brain or abscess should be considered.

WAGGONER, Ann Arbor, Mich.

THOROTRAST ENCEPHALOGRAPHY BY CISTERNA PUNCTURE. F. O. COE, L. S. OTELL and O. F. HEDLEY, M. Ann. District of Columbia **2**:277 (Dec.) 1933.

The authors present a preliminary report of experimental studies with the subarachnoid injection of thorium dioxide solution. The studies resulted from a search for a substance that would most closely conform to the requirements of an ideal agent for visualizing the cerebral ventricles and the subarachnoid spaces. Such an agent should be nontoxic and nonirritating, should cast a dense shadow, should be miscible with the cerebrospinal fluid and should be readily eliminated. Four monkeys were used. Two cubic centimeters of fluid was withdrawn from the cisterna, and 6 cc. of thorium dioxide solution was injected. This was done under the fluoroscope. It was observed that the thorium dioxide solution passed downward and upward as a diffuse opacity. The cerebral sulci, as well as the ventricles, were clearly outlined. Roentgenograms taken after thirty minutes showed even better visualization. Three of the monkeys died within twenty-four hours,

and the fourth was killed. In a series of five monkeys only 2 cc. of the solution was injected. The roentgenograms were practically as satisfactory as those for the first series. However, only one of the animals showed no ill effects; the others presented slight or severe hemiplegia. Roentgenograms taken after a week showed much of the thorium dioxide gone; at the end of four months only a slight residue was detected. The authors are enthusiastic over the roentgenographic results, but they think that the method is stlll too hazardous to warrant its use as a clinical procedure.

SCHNEIDER, Washington, D. C.

HYPNOSIS AND ALLIED FORMS OF SUGGESTION IN PRACTICAL PSYCHOTHERAPY. OSCAR J. RAEDER, Am. J. Psychiat. **13**:69 (July) 1933.

Although logical reasoning and persuasion are the methods of choice in the psychic treatment of intelligent patients, contact on a lower level must be established in many instances. Hypnotic suggestion has a definite but limited place in the armamentarium of the neuropsychiatrist. It owes its effectiveness to the fact that in every adult there persists some residuum of the suggestibility of the child. Once a patient focuses his attention enough to respond to suggestion, he becomes more suggestible. There are, however, varying degrees of suggestibility, such as light somnolence, the hypnoid state, the "hypnoidal state" of Sidis, light hypnosis and diverse intensities of dissociation reaching, at the extreme, states of total amnesia and dual personality. The milder states are more valuable to the psychotherapeutist than the more intense hypnotic phases. Treatment by this means will often prove of value in cases of alcoholism with obsessions and amnesia and in cases of true hysteria. The author reports three cases of treatment by suggestion. Hypnosis was induced by the method of Braid, or hypnoidization by the technic of Sidis. This was supplemented by suggestion during the waking state. Treatments lasted from ten to twenty minutes; a single hypnotic treatment was employed in two of the cases; several treatments were employed in the third case. One patient suffered from acute hysterical blindness, one from repeated fainting spells of neurotic origin and one from seizures of almost catatonic type. The exact procedure employed by the author in each case is described.

DAVIDSON, Newark, N. J.

CREATINURIA AMONG ADOLESCENT MALES. A. B. LIGHT and C. R. WARREN, J. Biol. Chem. **104**:121 (Jan.) 1934.

The authors report results from the study of twenty-four hour specimens of urine procured from adolescent boys in the Lawrenceville School, Lawrenceville, N. J., under various conditions of rest, exercise and diet. They found creatine in single twenty-four hour specimens of thirty-five of eighty-one normal boys between 14 and 19 years of age. The percentage showing creatinuria remained fairly constant at ages from 14 to 17 and dropped perceptibly between 17 and 18, while it was present in only one of six boys between 18 and 19. In one subject between 16 and 17, the excretion was 229 mg. in twenty-four hours. The average creatine excretion for each yearly period declines with increasing age. Five subjects showed far less creatine excretion while on a high protein diet and resting in bed than on the following day, when they were given a diet that was lower in protein while attending classes and engaging in exercise. Five of six subjects who had been confined to bed for either a minor illness or an injury showed a marked increase in the creatine excretion on the first day of muscular activity and a progressive decrease on each successive day.

This article is of immediate interest because of the prevalent impression that creatine is not found in the urine of normal males over 15 or 16 years of age, because of the large amount of work being done on creatine excretion in muscular atrophies and dystrophies and because of the effect of treatment with amino-acids in these diseases.

DAILEY, Boston.

PSYCHIATRY AND ITS RELATIONSHIP TO THE ADMINISTRATION OF THE CRIMINAL LAW. WILLIAM NELSON, Am. J. Psychiat. **12**:705 (Jan.) 1933.

The psychiatrist until recently has served in the criminal courts as the paid partisan of the defendant or the state; the orgy of hypothetic questions and cross examinations has tended to bring the profession into disrepute, befuddle the jurors and handicap the administration of justice. There is, however, a growing tendency to set up the psychiatrist as an impartial observer and as a real aid to justice. Paid by the state and serving as a part of the machinery of the administration, he can often furnish the court with a sensible understanding of the human forces involved in the crime and can give recommendations as to disposition which will point the way to the rehabilitation of the offender as well as to the protection of society. As illustration of the system described, Nelson reports the study of 410 defendants before various adult courts in Missouri, referred to him by attorneys, social agencies and judges. Of these 410 persons, only 7 (1.7 per cent) had normal mentality. However, the group is necessarily a highly selected one, since the agencies or persons referring the defendants perceived some gross suggestion of mental abnormality from even superficial contact. Thirty-six per cent of the persons suffered from frank mental disease, and 33 per cent from psychopathic personality. Twenty-three per cent had an appreciable degree of mental deficiency. The paper is illustrated by the citation of two cases of miscarriage of justice because of the refusal of the legal authorities to consider or carry out psychiatric recommendations.

DAVIDSON, Newark, N. J.

RELIEF OF PELVIC PAIN BY SYMPATHETIC NEURECTOMY: REPORT OF SEVEN CASES IN WHICH THE SUPERIOR HYPOGASTRIC PLEXUS (PRESACRAL NERVE) WAS RESECTED. F. S. WETHERELL, J. A. M. A. **101**:1295 (Oct. 21) 1933.

Wetherell reports seven cases in which relief from pelvic pain and from functional dysmenorrhea followed the resection of the superior hypogastric plexus (presacral nerve), as practiced for several years by various European surgeons. A midline incision was made extending from the symphysis pubic to or, better still, slightly above and to the left of the umbilicus. The pelvis was explored, and any gross pathologic conditions were treated in the usual manner. The sigmoid and the small intestine were packed off. The bifurcation of the aorta was palpated, and the parietal peritoneum was picked up just below it and nicked with scissors. The area of the superior hypogastric plexus was laid bare. Then, with the aid of blunt right-angled hooks, the fibers of the plexus were picked up and bluntly dissected with a small moist cotton ball on forceps. This dissection was carried upward to the beginning of the plexus and downward to the beginning of the inferior hypogastric nerves. The bundle of nerve fibers was resected at these points. All communicating fibers were cut during the resection, and the posterior parietal peritoneum was closed over the area. In a certain percentage of cases, difficulty may be encountered because of the implantation of the mesosigmoid to the right; but a small nick in the right leaf, which is then enlarged by careful tearing rather than cutting, results in a good exposure of the interiliac trigon.

EDITOR'S ABSTRACT.

MICROGLIA IN MONGOLIAN IDIOCY. F. CARDONA, Riv. di pat. nerv. **41**:293 (March-April) 1933.

The author has studied the reaction of microglia in two cases of mongolian idiocy with various histologic methods. He reports the absence of a progressive process in the microglia in the hypothalamic region and along the base of the cerebrum. On the other hand, he reports a slight increase of microglia cells in the gray matter of the cortex, particularly in the frontal and parietal regions. The increase is particularly noticeable in the most superficial strata of the cortex. Microglia cells do not show, however, regressive changes, either of the cell body

or of the processes, nor do they undergo transformation into rod cells or compound granular corpuscles.

On the basis of the reaction of the microglia, Cardona feels justified in supporting the conception that mongolian idiocy is an expression of a hypoplasia of the cerebral cortex; the absence of even the slightest reactive phenomena of microglia in the vegetative centers of the diencephalon seems to oppose the conception of Van der Scheer, who claimed that mongolian idiocy is a result of primary involvement of the subthalamic and diencephalic areas. Study of the microglia also does not support the theory of Babonneix, who attributed a considerable weight to syphilis in the pathogenesis of mongolian idiocy. If syphilis played a rôle, microglia would show manifestations of a progressive character if nothing else.

FERRARO, New York.

THE VALUE OF PSYCHOANALYSIS AS A THERAPEUTIC PROCEDURE. LEO KESSEL and H. T. HYMAN, J. A. M. A. **101**:1612 (Nov. 18) 1933.

Of their thirty-three cases Kessel and Hyman classify sixteen as failures. This group includes all the true psychotic patients and all the patients beyond the age of 40 at the time of their analysis. Seventeen of the patients were helped by psychoanalysis. In five instances the cure was specific. In the remaining patients the results were good but not startling, and at times the result was not specific but due to modified circumstances. Despite the narrow therapeutic range and the limitations, restrictions and criticisms of the analytic method and its practitioners, it is the authors' belief that the freudian school offers the only intelligent approach toward the successful management of many psychiatric problems. In a broader sense, the newer teachings have widely influenced one's manner of thinking and one's approach to many of the problems that one meets in everyday practice. It is in dealing with the individual patient that disappointment is so keen and criticism so often in order. The support of the movement as a whole and of the analyst as an individual has come for the most part from the public and from a few enlightened internists, such as the senior author. Faculties of medical schools and neurologists, in particular, many of the larger hospitals and medical centers have been and in many instances are still openly hostile to psychoanalysis.

EDITOR'S ABSTRACT.

STUDIES ON THE PHYSIOLOGY OF THE PARATHYROID GLANDS: IV. RENAL COMPLICATIONS OF HYPERPARATHYROIDISM. FULLER ALBRIGHT, P. C. BAIRD, OLIVER COPE and ESTHER BLOOMBERG, Am. J. M. Sc. **187**:49 (Jan.) 1934.

The three types of renal impairment, depending on the locus of precipitation, are: (1) pyelonephritis secondary to the formation of calcium phosphate stones in the renal pelves, (2) precipitation in renal tubules with resulting renal sclerosis, contraction and insufficiency and (3) acute parathyroid poisoning with anuresis, with deposits of calcium in the parenchyma of the kidneys and with resulting death. Cases of hyperparathyroidism with renal lesions are reviewed from the literature. The presence of a renal stone should suggest the possibility of hyperparathyroidism. Metabolic studies on two patients with type 2 lesions are discussed. In the prophylaxis against renal damage, fluids should be forced, an alkaline urine should be avoided, acidosis-producing salts are contraindicated, and a diet high in phosphorus and in calcium, while indicated for demineralization, imperils the kidneys and should be used only when the blood values can be carefully followed. Although temporary improvement in the condition of the bone may occur with medical treatment (one case), it is believed that all patients with hyperparathyroidism will eventually have renal damage unless there is surgical intervention.

MICHAELS, Boston.

RELATION BETWEEN NUTRITION, MENTAL LEVEL AND ADJUSTMENT IN DELINQUENT BOYS. MATTHEW MOLITCH and AUGUST K. ECCLES, J. Nerv. & Ment. Dis. **78**:123 (Aug.) 1933.

No positive relationship has been found to exist between good nutrition and behavior. By a new anthropometric technic the authors have undertaken a study of all the inmates of the New Jersey State Home for Boys at Jamesburg. Many children whom Molitch regarded as underweight were found to be average or above average weight when the width of their skeletal framework was taken into consideration. Negroes were found as a class to have narrow skeletal width, while Poles and Italians had a wide frame. The American white natives range between these two groups. Psychometric measurements were made with the Stanford-Binet, Kuhlman-Anderson, Morgan, Healy picture completion, Porteus maze and other tests

Eight hundred boys aged between 8 and 18 were studied according to the racial width-height index. From the psychologic standpoint a study of 554 cases revealed no significant difference in general mental level or in overt behavior between those who were well nourished and those who were undernourished. However, the undernourished group exhibited a shade of disadvantage in both mentality and quality of social adjustment. The writers thus substantiate the findings of Healy that the delinquent boy is not the undernourished boy.

HART, Greenwich, Conn.

STUDIES ON THE ADRENAL: III. THE PREPARATION OF AN ACTIVE EXTRACT OF THE HORMONE OF THE ADRENAL CORTEX. ARTHUR GROLLMAN and W. M. FIROR, J. Biol. Chem. **100**:429, 1933.

A method is described for preparing extracts of the suprarenal cortex which is simpler than the methods previously available. Suprarenal cortex is extracted with acetone and subsequently with benzene. The benzene solution is shaken with a saturated solution of sodium bicarbonate and then with normal hydrochloric acid, and finally 0.8 per cent saline solution is added and the benzene is removed in vacuo. The saline solution of the extract is filtered through a sterile Seitz filter. Extracts prepared in this way are odorless, colorless and water-clear, except in high concentration, and then they are faintly yellow. The low content of total solids, less than 1 mg. per cubic centimeter if distilled water is used, is evidence of the purity of the extracts prepared by this method. The toxicity resulting from chemical decomposition sometimes observed in extracts of the suprarenal gland made by other methods was not noted with these preparations, which are nontoxic and potent. The potency was determined by the maintenance of normal growth in suprarenalectomized young rats. Microscopic examinations revealed no residue of cortical tissue. One suprarenalectomized puppy is reported to have increased in weight from 1,980 to 3,300 Gm. in five weeks and to have been normal during this period.

DAILEY, Boston.

PHYSIQUE AND DEVELOPMENTAL ANOMALIES IN SCHIZOPHRENIA. W. PLATTNER, Arch. f. Psychiat. **98**:350 (Dec.) 1932.

Plattner studied one hundred cases of schizophrenia in males in whom the disease process had been of long duration. He found thirty patients of typical asthenic, sixteen of athletic, and eleven of pyknic build. The remaining patients were of dysplastic or mixed type, or persons in whom no typical physique was detected. In all the cases he found a large number of stigmas of degeneration and dysplasias. The most pronounced anomalies were present with an asthenic habitus, in which he found asymmetries of the skull and face, malformations of the thorax, kyphoses and scolioses of the vertebral column, feminine pelvis, poor growth of hair, cyanosis of the hands, and abnormalities of the genitals. These anomalies were much less pronounced in the athletic types, in which they were restricted mainly to the face and skull, frequently presenting acromegalic features. Abnormal-

ities in the distribution of hair were also pronounced in this group. In the pyknic types, too, there were few physical anomalies. The most pronounced were knock-knees, cyanosis or varicosity of the legs, and a tendency toward a feminine physical build. The anomalies in pyknic schizophrenic patients were, however, more pronounced than is usual in pyknic persons who develop manic-depressive psychoses. The author concludes that these stigmas point toward a constitutional factor in the causation of schizophrenia.

MALAMUD, Iowa City.

BLOOD CHOLESTEROL STUDIES IN MENTAL DISEASE: II. SCHIZOPHRENIA. PURCELL G. SCHUBE, Am. J. Psychiat. **12**:1227 (May) 1933.

Cholesterol constitutes 25 per cent of the dry content of the brain, and its share in lipoid metabolism seems essential to the normal functioning of that organ. The present paper is a report of cholesterol studies in fifty-five cases of schizophrenia. All but six showed values below the normal mean. Certain physiologic conditions, however, are associated with low cholesterol values. Among these are infancy and emaciation. Hypocholesteremia is also seen in jaundice and pernicious anemia. These conditions, however, were not found in the present series of patients. No correlation was found between cholesterol content, on the one hand, and body type, state of nourishment, blood picture, physical activity or physical abnormality, on the other hand. The normal range of cholesterol values in milligrams per hundred cubic centimeters of blood is from 110 to 195; the median is 150. The median in this schizophrenic group was 100. The cholesterol values in the normal group fell below the mean in 37 per cent; in the schizophrenic group, in 89 per cent. Of the patients in the latter group, the highest figures were obtained among the catatonic patients, with a median of 130 (the normal median is 150), and the lowest figures among the hebephrenic patients, with a median of 88. From this study, it appears that the cholesterol content of the blood of patients with schizophrenia is definitely below normal.

DAVIDSON, Newark, N. J.

STUDIES OF A FAMILY AFFLICTED WITH HUNTINGTON'S CHOREA. M. RIGGENBACH and A. WERTHEMANN, Schweiz. Arch. f. Neurol. u. Psychiat. **31**:306, 1933.

The authors present data relative to forty-eight members and five generations of the family which they investigated. Nine were known to have Huntington's chorea; ten either had died prior to the usual age of onset or had not attained that age. No descendant of the members not afflicted had contracted the disease. Contrary to the general rule, those remaining free from the disease were well equipped mentally and physically, several being of superior intelligence. The nine suffering from Huntington's chorea showed much the same clinical picture. All but one deteriorated mentally; in some instances mental and emotional changes constituted the first manifestations of the disease. The one case reported in detail is of some forensic interest since the patient killed his father four years after the appearance of choreiform movements. He was adjudged mentally incompetent and committed to a state hospital, where he died at the age of 48, seventeen years after the onset. Anatomically, the most marked changes were found in the small cells of the caudate nucleus and putamen; both of these structures were greatly shrunken. Extensive changes were also found in the middle layers of the cerebral cortex. The degree of glial response closely approximated the extent of damage to the ganglion cells.

DANIELS, Denver.

ISOLATED PARALYSIS OF THE MUSCLES OF THE BALL OF THE THUMB. G. DORNDORF, Monatschr. f. Psychiat. u. Neurol. **80**:331 (Oct.) 1931.

Dorndorf reports sixteen cases in which atrophy confined solely to the muscles of the ball of the thumb was observed. The condition occurred exclusively in women during or shortly after the menopause. The onset was gradual, and

the process came to a standstill within three or four years. The atrophy usually began in the muscles of the right thumb. In ten cases both thumbs were ultimately involved. As a rule, there was considerable impairment of function. Objective sensory alterations were not found, but paresthesia of the hands, arms and even other parts of the body was common. The abductor pollicis brevis and the opponens pollicis were affected regularly, the superficial head of the flexor pollicis brevis frequently and the deep head occasionally. In two instances the adductor pollicis was involved. The atrophy was invariably permanent, but the changes failed to spread to other muscles. Most of the patients were under observation for more than seven years. Half of the group showed signs of arteriosclerosis. In six cases local syncope of parts of the hand occurred. Dorndorf is inclined to believe that he is dealing with a uniform process. He suggests the possibility that the condition may be based on vasomotor disturbances which cause damage to the end-branches or end-organs of the motor nerves.

ROTHSCHILD, Foxborough, Mass.

CLINICAL CINEMATOGRAPHIC STUDY OF EPILEPSY AND THE PRINCIPLES OF THE ANALYSIS OF AN EXPERIMENTAL ATTACK. OTTO LÖWENSTEIN, Schweiz. Arch. f. Neurol. u. Psychiat. **32**:44, 1933.

Commonly accepted criteria may fail one in the differentiation of hysterical from epileptic seizures. Tongue biting, unless the lateral borders of the part are injured, is not an unequivocal sign of epilepsy, and immobility of the pupils has been observed in hysterical attacks. Löwenstein has been able to show, by means of cinematographic observations, that in certain persons the normal reaction of the pupil to light may be inhibited by either emotional stimuli or voluntary muscular exertion; further, that in these persons one may observe pupillary immobility during psychogenic seizures. Kymographic records of the motor reaction to emotional stimuli in persons with hysterical tendencies show a peculiar secondary response which may follow an entirely normal primary reaction. Tests of this sort, in doubtful cases, are as important as the hyperventilation test.

Since even trained attendants may give unsatisfactory descriptions of an attack, the author has devised an apparatus which permits the prompt taking of motion pictures of the patient whenever he has an attack. This apparatus has proved useful not only in differential diagnosis but also in the analysis of true epileptic attacks.

DANIELS, Denver.

THE CHRONOLOGICAL ORDER OF COMPRESSIONS OF THE NERVES IN TUMORS OF THE APEX OF THE ORBIT. JEAN SÉDAN, Rev. d'oto-neuro-opht. **11**:513 (July-Aug.) 1933.

Four cases of tumor of the orbit have been observed in which the nerves penetrating the sphenoid fissure were compressed in the same order. In all the cases the tumors have arisen at the level of the sella turcica or the small wing of the sphenoid bone. Anesthesia in the distribution of the frontal branches of the fifth nerve is the earliest sign and is often preceded by neuralgia affecting an area from 5 to 6 cm. wide just above the brow and extending to the occipitoparietal suture. Almost at the same time, paralysis of the third nerve appears, beginning with the fibers that supply the extrinsic muscles. After a period of from one to three months, paralysis of the sixth nerve appears, and then the fourth nerve becomes involved. Axial exophthalmos and compression of the optic nerve are the last to occur. Anesthesia and neuralgia of the frontal branches should warn the observer of serious trouble, and when paralysis of the third nerve occurs the diagnosis should be made and intervention undertaken. Roentgenography will give precise information. Ophthalmoscopic signs and lowering of visual acuity should not be waited for, since these signs appear late.

DENNIS, San Diego, Calif.

MUSCLE EXTRACT TREATMENT OF INTERMITTENT CLAUDICATION. MAURICE NEWMAN, Brit. M. J. **1**:611 (April 8) 1933.

Muscle extract has been used in various conditions, notably angina pectoris, thrombo-angiitis obliterans and intermittent claudication, to dilate the vessels and thus insure a better supply of blood. The author reports his experience with ten patients with intermittent claudication treated with muscle extract and an extract obtained from the pancreas. The exact chemical nature of these two preparations is still somewhat indefinite. The most important action of the extracts is the effect of vasodilatation on the arterioles of the periphery, and the dilatation of the coronary arteries. Of the ten patients with intermittent claudication, all except one showed some definite degree of improvement. The one exception had an advanced case of general arteriosclerosis with calcified arteries. The extract was first injected into the gluteus muscle; a course of six daily injections of one ampule was given, followed by 20 minims (1.25 cc.) of the extract by mouth, three times a day, for some weeks. Further courses of treatment were given until the maximum of improvement was obtained. The improvement in these cases was maintained for a period of at least six months, and several patients have been under observation for more than twelve months. Three illustrative cases are cited.

FERGUSON, Niagara Falls, N. Y.

COMBINED POSTENCEPHALITIC ATTACKS (NARCOLEPSY, CATAPLEXY AND OCULOGYRIC SPASMS). J. VADÀSZ, Schweiz. Arch. f. Neurol. u. Psychiat. **32**:154, 1933.

Vadàsz reports the case of a man, aged 31, who became subject to frequent attacks of an irresistible desire to sleep six weeks after the appearance of cataplectic seizures. The patient gained weight rapidly; his nocturnal sleep became disturbed and, seven months after the onset, he became subject to spasms of upward gaze. A loss of facial expression noted on the first examination later became more marked, along with the appearance of signs of involvement of the pyramidal tract. The drowsiness was relieved by treatment with ephedrine, but the cataplexy responded better to a hyoscyamine derivative. Large doses of atropine had a favorable effect on both symptoms and afforded complete symptomatic relief from the oculogyric spasms. Although the patient had sustained an injury to his head twenty months before the onset and had been treated for a primary syphilitic lesion ten years before, the narcoleptic symptoms were attributed to chronic encephalitis. The frequent association in this case of oculogyric spasm with cataplectic attacks seemed to furnish additional support for the view previously expressed that both phenomena represent varieties of somatic sleep.

DANIELS, Denver.

AETIOLOGY OF ACUTE RHEUMATISM. BERNARD SCHLESINGER, Brit. M. J. **1**: 697 (April 22) 1933.

The author believes that the old idea of a specific infection as an etiologic factor in rheumatism may have to be modified, and attention directed more away from the bacterium and focused more on the tissue reactions of the patient. The explanation which appears most hopeful is that of bacterial allergy, on the lines of serum disease. In a nonfatal microbic infection the responsible micro-organisms are attacked by certain tissue cells and broken down. The patient thus becomes cured of the infection, but during the process the body may become sensitized to these disintegrated products, consisting largely of nucleoprotein, and will react in characteristic fashion should a fresh invasion and disintegration of the same organisms take place. This tends to explain the fact that acute rheumatism, especially a relapse in old cases, nearly always follows a streptococcic "sore throat" after a silent period of from ten to twenty-one days. Many predisposing causes of rheumatism have been observed, and in considering these various fac-

tors it soon becomes apparent that there is no one predisposing cause, but a combination of many. Further research is required before the whole problem is completely elucidated.

FERGUSON, Niagara Falls, N. Y.

PARENCHYMATOUS CORTICAL CEREBELLAR ATROPHY (CHRONIC ATROPHY OF PURKINJE'S CELLS). HARRY L. PARKER and JAMES W. KERNOHAN, Brain. **56**:191 (July) 1933.

There are only eleven representative cases of parenchymatous cortical cerebellar atrophy in the literature. The clinical features and pathologic changes are reviewed. The disease is one in which there is a specific destruction of the Purkinje cell layer in the cerebellar cortex with preservation of all other structures. The case of a woman whose symptoms commenced at the age of 56 is described. She presented universal ataxia and incoordination. Although she also had pulmonary tuberculosis and bilateral carcinoma of the ovary, these were considered not to be causally related. Pathologically, the predominant feature was a diffuse and massive destruction of the Purkinje cells with preservation of the basket cells. There was no gross atrophy of the cerebellum itself. There was an excessive diffuse pigmentary change in many of the ganglion cells throughout the central nervous system. In considering the possible etiologic factors, which are probably multiple, it is suggested that there may be a relatively high degree of vulnerability of the Purkinje cells, especially after the fifth decade, when they are more readily affected by age and disease than the rest of the cerebellum.

MICHAELS, Boston.

PARASYMPATHETIC POISONS AND ACCOMMODATION. M. RISCHARD, Ann. d'ocul. **170**:218 (March) 1933.

Rischard has sought to determine the action on accommodation in human eyes of poisons that affect the parasympathetic system. He points out that the ciliary muscle is composed of two sets of fibers, one radiating (muscle of Brücke) and the other circular (muscle of Rouget). In criticizing the classic theories of accommodation he points out that Tscherning learned that when the lens in enucleated eyes was not in accommodation, it did not assume the spherical form spoken of by Helmholtz; the central area was convex, and the periphery was flattened. He believed that the flattening of the periphery was the result of traction produced by the contraction of the ciliary muscle, all the fibers of which, both longitudinal and circular, drew the suspensory ligament toward the periphery and posteriorly. He mentions the fact that Nicolai, Suter, Hess and others have demonstrated fallacies in the theories advanced by Tscherning. He states that anatomically the muscle of Brücke cannot draw the zonular fibers backward, and that the muscle of Rouget could not cooperate in this traction, as it is relaxed (*paralysé*) during accommodation.

BERENS, New York.

SOME OBSERVATIONS ON THE FIFTH AND SEVENTH CRANIAL NERVES. E. ARNOLD CARMICHAEL and H. H. WOOLLARD, Brain **56**:109 (July) 1933.

A review of the comparative anatomy of the fifth nerve indicates that the functions of crude sensation precede those of a discriminating quality. From the examination of ten cases of neuralgia of the trigeminal nerve (with treatment by injection of alcohol), it is thought that after the injection of alcohol the relief from pain is equal to, and the area of anesthesia is as complete as, that following surgical treatment. The problem as to why a number of patients lose the sense of taste on the anterior two thirds of the tongue after destruction of the gasserian ganglion on the same side is discussed. Pain on deep pressure was investigated by means of an algometer, and it is suggested that this sense is mediated by the fifth nerve. The efferent fibers in the facial nerve, other than those of the chorda tympani, subserve proprioceptive sensibility. Blushing is independent of the integrity of the fifth and sympathetic nerves. The presence of a pain pathway

in the oculomotor nerve, the facial nerve and the sympathetic nerve could not be demonstrated, so that the fifth nerve remains the nerve which conveys all painful impulses from the facial region.

MICHAELS, Boston.

FOCAL ENLARGEMENT OF TEMPORAL BONE AS SIGN OF BRAIN TUMOR. ROSS H. THOMPSON, J. A. M. A. **100**:1678 (May 27) 1933.

Thompson discovered, in adults, aged from 23 to 28, three instances of focal bulging of the squamous portion of the temporal bone, due to an underlying tumor of the brain, which afforded valuable information for diagnosis and operation. In two cases, the bulgings probably occurred in childhood. Two cases were due to large gliomatous cysts; one, to a meningeal fibroblastoma. Two cases were unilateral; the other was bilateral, producing a milder bulging of the opposite squama. The meningeal fibroblastoma, arising from the lesser wing of the left sphenoid bone, in addition to the bulging of the left squama, was associated with hyperostosis of the bones of the corresponding side of the face. There is an influence of the growth of the brain on suture closure and on the size and shape of the brain-case. The size and shape of the young plastic skull is especially influenced by direct pressure from an encroaching intracranial tumor in the region of the squama. The question arises as to whether or not a fibroblastoma of the base of the brain in the vicinity of the lesser wing of the sphenoid bone can produce hyperostosis of the facial bones of the ipsilateral side.

EDITOR'S ABSTRACT.

PARALYSIS OF THE DILATOR MUSCLES OF THE LARYNX. RAMADIER, LÉVY-DEKER and CHAUSSÉ, Rev. d'oto-neuro-opht. **11**:749 (Dec.) 1933.

Paralysis of the dilator muscles of the glottis and its differentiation from paralysis of the recurrent laryngeal nerve are discussed, and two cases are reported. In one, the paralysis was caused by neurosyphilis, and for a long time was the sole discoverable sign of syphilis, except the loss of the photomotor reflex; in the other case, the paralysis arose from syringobulbia. In both patients an emergency tracheotomy was necessary. In the first case, the suspected diagnosis of syphilis was confirmed by the subsequent development of an undoubtedly tabetic syndrome.

While it is true that undoubted cases of paralysis of the dilator muscles have occurred in typhoid fever, diphtheria, saturnism, certain peripheral lesions (cancer of the esophagus or of the thyroid body) and syringobulbia, a practical rule is the one expressed by the authors in 1922: "All paralysis of the dilators of the glottis which does not prove its origin is syphilitic," and the therapeutic corollary is to apply systematically to this cryptogenetic laryngoplegia the treatment for neurosyphilis, since this offers the only chance for cure.

DENNIS, San Diego, Calif.

THE OPERATIVE TREATMENT OF TRAUMATIC EPILEPSY. L. A. NIKOLSKAYA, Sovet. psikhonevrol. **9**:58 (Jan.) 1933.

Nikolskaya reviews the local pathologic changes of traumatic epilepsy and points out that the convulsions are usually caused by irritation of the cortex, caused by a scar at the site of injury. Surgical treatment in such cases has usually been unsuccessful in the past because there has been a tendency to replace the scar with fascia or fat. Both usually become organized, frequently undergoing a cystic degeneration and becoming another source of cortical irritation. The author reviews one hundred cases; six case histories are given in detail, and she describes the technic used in her clinic. No attempt was made to replace the defect in the tissues of the brain formed by the removal of the scar, as the expansion of the brain usually takes care of the space left. This occurs quickly. If the cavity is too large the sides may be approximated with light catgut. The dura mater is sutured over the wound, but the defect in the bone is not replaced. In these cases

the results were gratifying, with a total disappearance of symptoms even one or two years after the operation, when a follow-up study was made.

KASANIN, Howard, R. I.

ARACHNOIDITIS OF THE OPTIC NERVE: SYMPTOMS REFERABLE TO THE EYE BEGINNING WITH QUADRANTANOPIA OF THE RIGHT SUPERIOR TEMPORAL PART OF THE VISUAL FIELD. SCHIFF-WERTHEIMER, Ann. d'ocul. **170**:246 (March) 1933.

In 1931, Schiff-Wertheimer examined a patient who had quadrantanopia of the right superior temporal part of the visual field. The condition progressed to hemianopia, involving the right field and the macular region. Neurologic examination and examination of the spinal fluid gave negative results, and a diagnosis of cerebral tumor was excluded. Antisyphilitic treatment did not prevent further loss of visual acuity. The progress was checked by roentgen therapy. In March, 1932, vision in the right eye was 1/20, and that in the left eye was limited to the perception of light. During an operation on the right frontal parietal region arachnoiditis was found involving the optic nerve and extending backward. Following the operation vision improved in the right eye to 8/10 and in the left eye to 3/10, but the hemianopia persisted. The patient evidently had localized arachnoiditis involving the optic tracts or the occipital region.

BERENS, New York.

SURGICAL CONSIDERATIONS OF CARCINOMATOUS METASTASES TO THE BRAIN. ERIC OLDBERG, J. A. M. A. **101**:1458 (Nov. 4) 1933.

Oldberg reports three cases of carcinomatous metastases to the brain in which the periods of survival following intracranial operation are longer than in previously reported cases. These periods of survival compare favorably with the results obtained from operations on relatively benign primary tumors of the brain. One case of suspected carcinomatous metastasis to the cervical cord is reported in which operation disclosed and made possible the removal of a meningioma, with recovery of the patient. The author suggests that operation on suspected malignant metastases to the brain, provided the general condition of the patient warrants it and that the cerebral lesion is apparently single, be undertaken for the following reasons: 1. It may be possible to extirpate the metastasis, with great relief to the patient and with prolongation of his life expectancy. 2. If the lesion cannot be removed, at least palliative decompression can be performed for the relief of distress. 3. Occasionally a gratifying surprise may be encountered in the form of a benign tumor, and no person should be refused this possibility.

EDITOR'S ABSTRACT.

SODIUM SALT OF BUTYL-ETHYL-BARBITURIC ACID AS A BASAL HYPNOTIC. S. E. BIRDSALL, Brit. M. J. **1**:871 (May 20) 1933.

The sodium salt of butyl-ethyl-barbituric acid has been used as a basal hypnotic for general anesthesia in 150 cases at St. Bartholomew's Hospital. Chemically it resembles sodium pentobarbital, which is sodium-ethyl-barbiturate; clinically it is of lower toxicity. The author's conclusions are that it is a reliable basal narcotic, producing sleep or drowsiness in 95 per cent of cases when administered by mouth one hour before the induction of general anesthesia. The optimum dose varies from 0.6 to 0.9 Gm., according to the patient's weight. Depression of respiration is produced in a few instances, and restlessness occurs in about 10 per cent of cases. No other toxic effects have been observed. The series of cases included patients whose ages varied from 6 to 70 years, and the operations performed were for diseases involving almost every part of the anatomy. It was not administered in cases of senility, pulmonary disease, renal impairment or arteriosclerosis.

FERGUSON, Niagara Falls, N. Y.

PSYCHOLOGY OF PROGRESSIVE DEAFNESS. GORDON BERRY, J. A. M. A. **101**:1599 (Nov. 18) 1933.

Berry discusses the psychology of progressive deafness from the point of view of one who is himself hard of hearing. Under changes in behavior as deafness progresses he deals only with the behavior changes through different ages (childhood, adolescence, young adult life, the prime of life and advanced years). Under adjustments he discusses mechanical and vocational measures, social adjustments and assurance. He states that impaired hearing may be an asset rather than a liability, as a handicapped laborer who knows a trade will tend to remain on the job and not leave in search of an easier and better paid task. Three assets may be mentioned: (1) Deafness decreases distractions and increases concentration, (2) it fosters constructive thought, though unfortunately the person may not have the creative genius to respond, and (3) it can and in some cases it does increase the interpretative capacity of the other senses. The author presents what he calls the nine commandments of the hard of hearing, which try to epitomize the philosophy of that hard of hearing man or woman who endeavors to face and surmount his handicap.

EDITOR'S ABSTRACT.

PSYCHIATRIC FUTURES. EDWARD A. STRECKER, Ment. Hyg. **17**:569 (Oct.) 1933.

The level of the intelligence and the mental soundness of the thinking of a group cannot rise above the level of those of its average members. The body politic, therefore, seems to suffer from the neuroses to which individual members are susceptible and seems to employ the psychiatric mechanisms of escape common among patients. The frenzied activities of prosperity represent merely the aggregate of the euphoric sentiment of the members of the community. The tendency of a nation to blame another nation for its difficulties, and the spectacle of one racial or vocational group ascribing its difficulties to the stubbornness or malice of another suggest a projection mechanism on a large scale analogous to the corresponding process of individual behavior. The apparent inability of the world to learn anything from war or other disasters is similar to the well recognized purposeful forgetting which is called repression. One cannot, therefore, expect intelligent economic or social management on a large scale until individual persons are taught to master themselves.

DAVIDSON, Newark, N. J.

PSYCHIATRY AS APPLIED TO CRIMINOLOGY IN THE UNITED STATES. HERMAN ADLER, J. Crim. Law & Criminol. **24**:50 (May-June) 1933.

In only twenty-five years psychiatry has changed from being primarily concerned with mental disease and the care of patients in hospitals for mental diseases to occupying itself increasingly with motivations and deviations of behavior. Some of the more important steps in this change were the founding of the Juvenile Psychopathic Institute and the opening of the Boston Psychopathic Hospital and of the Phipps Psychiatric Clinic. Now, many medical schools give courses in criminology; there are many psychiatrists working on the problems of criminology, and the American Bar Association as well as other similar groups are interested. The work of Binet and Freud, as well as war-time needs, gave impetus to the work. Indications seem to be that in the future fact-finding in regard to the prisoner's guilt or innocence will be separated from the punishment or treatment to be applied and that the psychiatrist will have a definite responsibility to the community in the treatment for crime.

SELLING, Chicago.

SELF-MUTILATION IN CHRONIC ENCEPHALITIS. AVULSION OF BOTH EYE-BALLS AND EXTRACTION OF TEETH. S. P. GOODHART and NATHAN LAVITSKY, Am. J. M. Sc. **185**:674 (May) 1933.

The case is reported of a girl, aged 16, with chronic encephalitis, who suddenly gouged out both eyes and, during a period of about two years, pulled out all

but seven of her own teeth. In the medical literature there are recorded only four cases in which both eyes were avulsed; the case here reported is the only one of self-blinding with chronic encephalitis. Some of the psychopathologic aspects of self-blinding are mentioned (the psychoanalytic formulation of self-castration). The self-mutilation tendencies in the patient are considered as compulsion phenomena. Although compulsion phenomena have frequently been described in chronic encephalitis, the rarity of compulsions to self-mutilation in encephalitis is striking. The questions of amnesia and transitory affection of the pain perception mechanism are discussed. It is hoped that the detailed psychodynamic features of this case will be reported further. MICHAELS, Boston.

LIVER INJURY AND BLOOD LACTIC ACID. PAUL F. HAHN, J. Biol. Chem. **101**:29 (June) 1933.

There has been no agreement as yet as to the value of any test of hepatic function. The liver can be severely damaged without decrease in its glycogenic or urea-forming functions. Hahn hoped that there might not be such a large margin of safety for the elimination of lactic acid and that the metabolism of the liver might be measured by the rate of removal of lactic acid from the blood. The results show conclusively that this procedure is of no value for the determination of hepatic function. When considerable amounts of lactic acid or sodium lactate are injected intravenously into normal dogs, there is a rapid disappearance of this substance from the blood stream. When the liver has been severely injured by chloroform poisoning, the disappearance curve for lactate in the blood is similar to the curve recorded in the normal dog. If the liver is normally concerned with the removal of lactic acid from the blood, some emergency alternative reaction comes into play when the liver is functionally disturbed or incapacitated.

DAILEY, Boston.

PRESENT STATUS OF VARIOUS SPINAL ANESTHETICS AND THEIR CLINICAL USEFULNESS. F. W. MARVIN, J. A. M. A. **101**:1475 (Nov. 4) 1933.

After a careful survey and use of several drugs, Marvin confined his study to procaine hydrochloride, neothesin (benzoylgamma [2-methylpiperidine] propanol hydrochloride), nupercaine and pantocaine (p-n-butyl-amino-benzoyl-dimethyl-amino-ethanol hydrochloride) at the Boston City Hospital during the past sixteen months without a fatality. These drugs have been used separately and in different combinations for very definite purposes, with the result that he has formed a strong opinion that it is not necessary to mix them. He advises the use of them separately for each individual case. Procaine hydrochloride and pantocaine are the drugs frequently employed. Of these two drugs, pantocaine offers everything that procaine hydrochloride will accomplish and has the advantage that it does *not* lower the blood pressure as does procaine. Furthermore, clinically, it is apparently less toxic than procaine hydrochloride, besides producing a longer and more satisfactory anesthesia. EDITOR'S ABSTRACT.

CHRONIC DEFORMING ARTHRITIS. MARIO BERGONZI, Riv. di path. nerv. **41**:162 (Jan.-Feb.) 1933.

Bergonzi reports, from the clinical and histopathologic standpoint, a case of chronic deforming arthritis in which the roentgen and anatomic findings of the bony and articular structures are classic. Histologic examination disclosed evidence of inflammatory and degenerative changes of the peripheral nerves and of the spinal ganglia, as well as degenerative lesions of bundles of fibers in the posterior columns. The author considers the changes as secondary to the arthritis. However, there were disclosed also by histologic examination changes of the cellular elements of the nucleus paraventricularis and nucleus supra-opticus in the subthalamic region, a certain degree of sclerosis of the testis, with diminution and

degenerative changes of the Leydig cells, a still functioning epiphysis and hypothyroidism. The author tries to correlate these changes with the fundamental process of chronic deforming arthritis.

FERRARO, New York.

THE CEREBROSPINAL FLUID AND THE CERVICAL LYMPH NODES. O. A. MORTENSEN and W. E. SULLIVAN, Anat. Rec. **56**:359 (July 25) 1933.

The passage of the cerebrospinal fluid into the venous sinuses and into the cervical lymph nodes has been demonstrated by Key and Retzius and by Weed and his co-workers. Now, Mortensen and Sullivan demonstrate in the living animal by two agents, brominized oil and thorium dioxide, that foreign material introduced into the subarachnoid space passes readily into the cervical lymph nodes, both superficial and deep. Their experiments were made on dogs. From 2 to 3 cc. of fluid was removed by cisternal puncture and replaced by an equal amount of thorium dioxide or brominized oil. The injected substance diffused around the cerebral cortex and the base of the brain, particularly in the region of the optic nerves, and passed into the deep cervical nodes by way of the nasal cavity. Thorium dioxide is transferred more rapidly than brominized oil and is more satisfactory from the standpoint of roentgenology.

DAILEY, Boston.

OLD AND RECENT STUDIES OF CENTRIFUGAL FIBERS IN THE POSTERIOR ROOTS. E. LUGARO, Schweiz. Arch. f. Neurol. u. Psychiat. **31**:284, 1933.

Using the osmic acid and Cajal methods of staining, Lugaro was able to show that the centrifugal fibers persisting in the posterior roots after ablation of the spinal ganglia were all amyelinated. This is contrary to the results of Ken Kuré and his co-workers, who, relying entirely on the Weigert stain, concluded that the fine centrifugal fibers were myelinated. The myelinated fibers present at times after removal of the ganglia either are aberrant, coming from adjacent uninjured roots, or, in the case of the sacral roots, arise from ectopic cells lying proximal to the main ganglia. Amyelinated fibers found in the extradural portion of the posterior roots after removal of the ganglia are centripetal and apparently come from sympathetic ganglia. Fine myelinated fibers present in the intradural portion some months after ablation are the products of regeneration.

DANIELS, Denver.

MULTIPLE FIBROMAS: RECKLINGHAUSEN'S DISEASE. JAMES T. WAYSON, Arch. Dermat. & Syph. **27**:421 (March) 1933.

A Chinese woman came to Hawaii at the age of 20. At that time her skin was without blemish. Shortly after her arrival, a few small tumors appeared. These increased in size and number until, thirty years later, she had thousands of fibromas. There were hundreds on the scalp and face, and many on the lips. The palms and soles and the interdigital spaces in all four extremities were covered with lesions. The patient had four children; the two sons and one of the daughters had numerous lesions. The other daughter, although free from tumors, had a goiter. A child born to the daughter with the fibromas had large fontanels and was unable to raise its head when 9 months of age. The author does not state whether a biopsy was done and what the pathologic study, if any was made, showed.

DAVIDSON, Newark, N. J.

THE EFFECTS OF X-RAYS ON ANTERIOR REGENERATION IN TUBIFEX TUBIFEX. RAYMOND G. STONE, J. Morphol. **54**:303 (March 5) 1933.

A head region consisting of two segments and the prostomium is regenerated in Tubifex if not more than twelve anterior segments are removed. The epidermal and nerve tissues of the regenerated segments arise by proliferation of the epidermis, the pharynx by transformation of the anterior end of the intestine and

the muscle layers by migration of cells from the old muscle elements. Anterior regeneration is completely inhibited by sufficient exposure to the x-rays. In irradiated worms there is no proliferation in the epidermis, and the cerebral ganglia are not replaced. This failure of regeneration is thought to be due to chemical changes within the cells of the anterior region which result in their altered behavior.

WYMAN, Boston.

STATISTICAL STUDIES ON THE ETIOLOGY AND AGE OF ONSET IN EPILEPSY WITH PARTICULAR CONSIDERATION OF EPILEPTIC TWINS. GERTRUD STROESSLER, Schweiz. Arch. f. Neurol. u. Psychiat. **32**:115, 1933.

Although 45 of 4,280 epileptic patients whose records were reviewed by Stroessler were twins, identical twins were encountered only twice; these and a pair of biovular twins furnished the only instances of epilepsy in both members of a pair. The average age at onset (13 years) and the proportion of cases of symptomatic epilepsy were approximately the same among the twins as in the entire series. Twin birth did not appear to predispose to epilepsy. A family history of epilepsy was obtained in 22.6 per cent of the 4,280 cases, but direct antecedents, that is, parents or grandparents, were known to have had seizures in only 6 per cent of the cases.

DANIELS, Denver.

COMPLETE DISAPPEARANCE OF TYPICAL BITEMPORAL HEMIANOPIA; THE RESULTS OF RADIOTHERAPY IN CASES OF TUMOR OF THE HYPOPHYSIS. HAMBRESIN, Ann. d'ocul. **170**:89 (Jan.) 1933.

In the treatment of tumors of the hypophysis it is always wise to begin by using radiotherapy, but it should be remembered that the action of the rays is manifest after the first few treatments, when the tumor is sensitive to the rays. If no improvement is noted at the end of a month it is useless to continue. Hambresin points out that radiotherapy is not as inoffensive as one might believe, and that its results are far from definite in the majority of cases. He foresees the time when, because of the perfection of technic, surgery will be the most efficacious treatment for tumors of the hypophysis.

BERENS, New York.

THE USE OF VARIOUS GASES IN ENCEPHALOGRAPHY. A SUMMARY OF TWO HUNDRED AND TEN CASES USING THE SIMULTANEOUS DISPLACEMENT APPARATUS. F. LIBERSON, Am. J. M. Sc. **185**:478 (April) 1933.

With the principle that "fluid will seek its level," a good apparatus was devised so that successful encephalography was performed in the cases of 210 patients, without fatality or serious accident. Although the shock reaction occurred infrequently, headache was almost a constant accompaniment. With filtration of the gas used in encephalography there was less meningeal reaction. The author experimented with various gases—air, carbon dioxide, nitrogen and helium. Although helium was used in only 12 cases, the results were encouraging enough to suggest its continued trial in the future.

MICHAELS, Boston.

BILATERAL CERVICAL CHORDOTOMY: FOR RELIEF OF PAIN IN CHRONIC INFECTIOUS ARTHRITIS. M. M. PEET, E. A. KAHN and S. S. ALLEN, J. A. M. A. **100**:488 (April 15) 1933.

The authors present a case of chronic arthritis that required the control of pain in both lower extremities and, in addition, in the right arm and shoulder. The pain was abolished without risk of respiratory paralysis by sectioning the tract at the third cervical segment on one side and approximately the eighth cervical segment on the other. This produced the greatest area of analgesia in any patient of their series of seventy patients on whom anterolateral chordotomy

has been performed in their clinic. Foerster's case is the only one in the literature in which they have found that a greater area of analgesia has been obtained.

EDITOR'S ABSTRACT.

NEUROLOGIC COMPLICATIONS OF SERUM SICKNESS. J. B. DOYLE, Am. J. M. Sc. **185**:484 (April) 1933.

Doyle has tabulated from the literature forty-seven apparently authentic examples of neurologic complications of serum sickness. The majority of the cases were in adults (average age, 26.9 years) and in males. In thirty-five cases the average interval between the onset of serum sickness and the appearance of neurologic complications was approximately two days. Tetanus antitoxin was the serum most frequently followed by neurologic complications. In the majority of cases structures of the brachial plexus were involved (motor in all the cases; sensory in one fourth of the cases). In view of the general rarity of neurologic complications, however, there is no contraindication to the judicious use of serums.

MICHAELS, Boston.

CONTAGIOUSNESS OF TRACHOMA: THREE RECENT CASES OF DIRECT CONTAGION: CONTAMINATION OF PHYSICIANS BY PATIENTS AFTER PERFORMANCE OF OPERATIONS. CUÉNOD and R. NATAF, Ann. d'ocul. **170**:78 (Jan.) 1933.

Cuénod and Nataf observed three physicians who contracted trachoma after having operated under identical circumstances. Infection was accidental and direct, and developed in eyes which were formerly normal. Morax stated that such instances of accidental inoculation are interesting since they are real experiments. There is no reason for infection other than by the still unknown agent of trachoma. By regular observation of the native children of an Egyptian village, Wilson proved the early appearance of trachoma in the absence of acute infections caused by Weeks' bacillus or by a diplobacillus.

BERENS, New York.

ACUTE MYELITIS (MYELOMALACIA): SYNDROME OF OCCLUSION OF ANTERIOR SPINAL ARTERY AT FIFTH CERVICAL CORD SEGMENT. W. F. SCHALLER, A. M. ROBERTS and E. F. STADTHERR, J. A. M. A. **99**:1572 (Nov. 5) 1932.

Two cases of acute myelitis illustrating the syndrome of occlusion of the anterior spinal artery at the fifth cervical cord segment are recorded. The authors discuss in detail the circulation of the spinal cord and point out that extensive acute myelitis occurring in the lower segments of the cervical cord produces a definite clinical picture: flaccid paralysis of the upper extremities with subsequent atrophies and contractures, spastic paralysis of the trunk and lower extremities and impairment of pain and temperature sensibility below the level of the lesion.

EDITOR'S ABSTRACT.

CONGENITAL HEMIHYPERTROPHY: A REPORT OF EIGHT CASES. E. G. WAKEFIELD and E. A. HINES, Am. J. M. Sc. **185**:493 (April) 1933.

Until 1926, in the literature of the Surgeon-General's Library, there were reports of 195 cases of congenital hemihypertrophy. In the 8 cases here reported, the right side was hypertrophied in 4, the left in 3 and in 1 the hypertrophy was crossed. It would have been of interest if the handedness had been determined in these cases. The mental status in 6 cases was normal; in 4 cases other congenital anomalies were present. Usually obvious unilateral enlargement of a part or parts is of casual significance to a patient until something has gone wrong. The etiology of this condition still remains unknown. The prognosis depends on the degree of hypertrophy and the age of the patient.

MICHAELS, Boston.

SYNDROME OF THE NASAL NERVE. WIBO, Ann. d'ocul. **170**:169 (Feb.) 1933.

In a study of neuritis of the nasal nerve, Wibo enumerates the characteristic features as follows: (1) a well marked inflammatory lesion of the anterior segment of the eye; (2) severe neuralgic pains in the orbitonasal regions of the same side, but with elective localization at the root of the nose and in the ala on the side corresponding to the inflamed eye; (3) a copious hydrorrhea, which accompanies the paroxysmal crises. Only an accurate knowledge of the anatomy of this region can clarify the symptomatology of this disease. After having eliminated various diagnoses, Wibo suggests that the cause is neuritis of the nasal nerve. Cocaine and epinephrine applied to the nose produce rapid and complete relief.

BERENS, New York.

THE USE OF EPHEDRIN DURING SPINAL ANAESTHESIA FOR THE RELIEF OF PARALYTIC ILEUS. A THERAPEUTIC FALLACY. A. M. WINOGRAD, D. A. HIRSCH and R. D. BARNARD, Am. J. M. Sc. **185**:506 (April) 1933.

In four anesthetized dogs with absence of intestinal motility, which returned with the introduction of a solution containing procaine and strychnine, there was a concurrent fall in blood pressure. The administration of ephedrine caused resumption of the original blood pressure but an immediate cessation of the intestinal motility. Thus, the authors believe that the use of ephedrine as a pressor substance in spinal anesthesia, when the latter is initiated for the relief of paralytic ileus, is contraindicated.

MICHAELS, Boston.

SURGERY OF THE SYMPATHETIC. F. ORBAN, Ann. d'ocul. **170**:87 (Jan.) 1933.

"The new surgery of the sympathetic is young and therefore incoherent; it lacks exact anatomic and physiologic bases, but it is rich in visible and indisputable clinical accomplishments." If the facts do not conform to classic physiology, it matters little, because they do exist. Orban, after paying tribute to his teacher Delrez and to F. Albert, who were the first to fix the fundamentals of pathologic physiology of the sympathetic for clinical cases, wrote an article on this subject. Surgery to relieve pain and that of the vasomotor and trophic systems are discussed in turn. Orban also states that his ideas are essentially those of Leriche, with whom he worked for a long time.

BERENS, New York.

PERVERSE PUPILLARY REACTIONS. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **10**:733 (Dec.) 1932.

A case of reversal in the reaction of the pupils in convergence was observed. Reports of only five other such cases were found in the literature. The name "perverse" was given to this phenomenon since "paradoxical" is applied to the reversal of the photomotor reaction. The patient, a woman, aged 50, presented no clinical or serologic evidence of tabes. Neither pupil reacted to light or consensually. In convergence the left pupil dilated while the right pupil contracted slightly. Antisyphilitic treatment had never been instituted.

DENNIS, San Diego, Calif.

CORNEAL COMPLICATIONS IN HERPES ZOSTER OPHTHALMICUS. J. ROLLET, Ann. d'ocul. **170**:78 (Jan.) 1933.

Rollet emphasizes the importance and frequency of deep interstitial lesions in herpes zoster ophthalmicus. These lesions were examined with a slit lamp and were found to be concomitant with superficial lesions. The corneal injuries appear most often in a diffuse form, and pure superficial forms are probably more rare than pure interstitial forms. The deep lesions really belong to the disease and are not the result of secondary infections. In biomicroscopic examinations in these cases Rollet has never found true vesicles; however, he does not deny their existence.

BERENS, New York.

THE INCIDENCE OF THROMBO-ANGIITIS OBLITERANS IN BROTHERS. SAUL S. SAMUELS, Am. J. M. Sc. **183**:465 (April) 1932.

The author reports the finding of three families, in the examination of over five hundred cases, in which the disease occurred in brothers with no direct evidence of inheritance. In two families, three brothers were affected; the parents in one family were born in Austria, and in the other they were Russian Jews. The third family, in which two brothers were affected, came from Austria. Again attention is called to the uniqueness of the disease, its predominance in Jews, its predilection for young males and its association with cigaret smoking.

MICHAELS, Boston.

PROGRESSIVE PARALYSIS OF THE THIRD, FOURTH, FIFTH AND SIXTH NERVES OF THE LEFT EYE ASSOCIATED WITH HOMOLATERAL ARGYLL ROBERTSON PUPIL. TERRIEN and P. DUPUY-DUTEMPS, Ann. d'ocul. **170**:250 (March) 1933.

A patient with progressive paralysis of the third, fourth, fifth and sixth nerves of the left eye associated with a homolateral Argyll Robertson pupil was examined by Terrien and Dupuy-Dutemps. As the cerebrospinal fluid was normal and the roentgenograms showed nothing abnormal, the authors thought that chronic meningitis at the base or a new growth was the most probable cause of the ocular changes.

PERSISTENT PAINS IN HERPES ZOSTER OPHTHALMICUS. BADOT, Ann. d'ocul. **170**:168 (Feb.) 1933.

Independent of medical treatment and of classic electric treatment for the persistent pain of herpes zoster, Badot advises one of the following methods: an injection of 80 per cent ethyl alcohol in the course of the nasal, frontal or lacrimal nerves, neurorrhaphy of the infra-orbital and supra-orbital nerves, injections of 1 per cent benzoyl-dimethyl-amino-ethylpropanol hydrochloride or of procaine hydrochloride, alcoholization of the gasserian ganglion or section of the posterior root.

FRACTURE OF THE OPTIC CANAL. P. BONNET, Ann. d'ocul. **170**:80 (Jan.) 1933.

Bonnet observed a case in which fracture of the optic canal was associated with an external fracture of the malar bone. Roentgenograms showed a fracture of the roof of the orbit. It was a fracture shaped like a ring surrounding the optic canal, with an indented line modifying its contour. The left eye was totally blind. This patient was observed daily and on the third day the fundus was normal. From the fifth day there was pallor of the temporal segment of the disk.

THE VISUAL FIELD IN STEREOSCOPIC VISION. A. ALAERTS, Ann. d'ocul. **170**: 343 (April) 1933.

Alaerts demonstrated different stereoscopic photographs, proving that they are not entirely superposable. Stereoscopic photographs are superposed exactly only at the point fixed; all others are imperfectly superposed, and this is most marked in the periphery of the field, which is most important for stereoscopic vision. Therefore, the essential factor for stereoscopic vision is a normal visual field.

STUDIES OF THE PATHOGENESIS OF BILATERAL PARALYSIS OF THE OCULOMOTOR NERVE OF TRAUMATIC ORIGIN. J. ROLLET, Ann. d'ocul. **170**:250 (March) 1933.

In his study of the pathogenesis of bilateral paralysis of the sixth nerve of traumatic origin Rollet has shown that the involvement of the nerve may be due either to direct trauma or to indirect involvement through lesions of the blood vessels.

A Case of Meningioma Diagnosed by Roentgenograms. Marbaix, Ann. d'ocul. **170**:169 (Feb.) 1933.

Marbaix reports a case of meningioma in which the first symptom was an acute retrobulbar neuritis caused by a cerebral condition, which had been developing for over five years. Marbaix insists on stereoscopic roentgenograms for the purpose of cerebral localization.

Anatomy and Pathology of the Discoid Degeneration of the Posterior Pole of the Eye. C. Behr, Ann. d'ocul. **170**:91 (Jan.) 1933.

The true nature of senile exudative retinitis is not known. Behr states that the principal cause of the condition is a senile modification of the elastic membrane of the choroid. He bases this conclusion on the examination of an eye enucleated because of sarcoma of the choroid.

Herpes Zoster Ophthalmicus with Paresis of the Ocular Muscles Associated with Retrobulbar Optic Neuritis of the Same Side. G. Leplat, Ann. d'ocul. **170**:337 (April) 1933.

Leplat examined a case of herpes zoster ophthalmicus with paresis of the ocular muscles, associated with retrobulbar optic neuritis on the same side, in which a syndrome of the sphenoid fissure developed.

A Case of Congenital Absence of Lateral Movements of One Eye (Syndrome of Stilling). H. Coppez, Ann. d'ocul. **170**:337 (April) 1933.

A case of fibrosis of the lateral and medial rectus muscles of the eye is discussed by Coppez. He believes that these cases should be named "syndrome of Stilling" after the author who first described this anomaly.

Angiospastic Papillary Anemia in Pregnancy. Tuyl, Ann. d'ocul. **170**: 346 (April) 1933.

Papillary anemia may be the first and only preeclamptic objective symptom. It may lead to atrophy, and its presence during two or three months sometimes may necessitate abortion.

Presenile Presbyopia and Poliosis. N. Blatt, Ann. d'ocul. **170**:350 (April) 1933.

After having observed twenty-five cases, Blatt affirms that there is a correlation between poliosis and presenile presbyopia. He believes that this correlation rests on a congenital heredofamilial degeneration of the ectodermal tissues.

Two Cases of Latent Nystagmus. Bailliart and Rossano, Ann. d'ocul. **170**:78 (Jan.) 1933.

In the case of a patient, aged 54, Bailliart and Rossano observed that nystagmus appeared when one eye was occluded by means of a screen.

Berens, New York.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, April 4, 1934

HENRY ALSOP RILEY, M.D., *President, in the Chair*

INFECTIOUS AND INFLAMMATORY DISEASES OF THE CENTRAL NERVOUS SYSTEM TREATED BY FORCED DRAINAGE

PRESENTATION OF CASES. DR. KATE CONSTABLE.

CASE 1.—A man, now aged 35 (from the New York Neurological Institute, Drs. Tilney and Constable), in 1926, at the age of 29, presented the first signs of slowly and irregularly progressive multiple sclerosis. Late in November 1932, there was an acute exacerbation, and within two or three days the patient was unable to walk or write. Examination showed spastic weakness with marked ataxia. On admission to the Neurological Institute on December 10, he was practically helpless. Forced drainage was done at once, with the intravenous injection of 1,125 cc. of 0.5 per cent saline solution and the removal of 105 cc. of cerebrospinal fluid. On the following morning he walked half the length of the hospital corridor. Four days later a second drainage was done with the injection of 1,800 cc. of saline solution in three and a half hours and the withdrawal of 165 cc. of cerebrospinal fluid. The patient had improved so much by January 1 that he was able to return to work. The right leg, formerly the weaker, seemed the stronger, and he was again able to write. In February, a third drainage was done, with the injection of 2,335 cc. of saline solution intravenously and the administration of 2 liters by mouth in five and a half hours and the withdrawal of 170 cc. of spinal fluid. He reported at the end of July 1933 that writing was normal and sensation in the hand unimpaired, that he had a slight feeling of unsteadiness, especially when hurried, but that he could walk several blocks without undue fatigue. The feeling of the legs being "incased in rubber" that he formerly had had entirely disappeared within two months after the last drainage. When last seen in April 1934, the patient reported that his main complaint was a feeling of stiffness in the arms and legs, but that otherwise his condition was unchanged. Examination showed spastic ataxia, with fairly good muscle power, slight terminal tremor in the left arm, absence of abdominal reflexes, increased ankle reflexes, a bilateral Babinski sign, diminished vibratory sense below the ankles, normal optic disks and no nystagmus.

The initial response to drainage was dramatic and convincing, and the gain has lasted over a year. It will be interesting to discover whether a like response can be obtained in case another exacerbation of symptoms should occur.

CASE 2.—A woman, aged 33, married, with one child, had an attack of acute encephalitis, the date of which is uncertain. Parkinsonian symptoms appeared insidiously seven years after the most recent suspicious illness. In the four years following their onset, the symptoms gradually increased. When first seen, the patient complained of pains in the lower part of the back, fatigability, trembling in the left hand, attacks of confusion and dazed feelings, slowed movements, staring gaze and irregularly recurring attacks of diplopia.

Examination revealed the parkinsonian mask, rhythmic tremor of the left arm and hand, which increased on effort, and tremor of the protruding tongue.

Forced drainage was done three times, the first two a week apart, and the third five months later. Between 2,300 and 3,100 cc. of 0.45 per cent saline solution was given intravenously in two and a half or three hours, with the withdrawal of

between 100 and 150 cc. of cerebrospinal fluid. After the first two treatments most of the facial masking disappeared, and the movements became free, although the tremor in the left hand and arm remained the same. The third treatment was followed by further similar improvement, although the attacks of confusion continued to recur two or three times a week.

CASE 3.—A girl, aged 17 (New York Neurological Institute, Drs. Tilney and Constable), in the summer of 1931, after a winter of recurrent sore throats with arthritic pain, noted a mild choreiform twitching of the right hand and arm. Despite occasional rest in bed and the administration of phenobarbital, this persisted throughout most of the winter of 1931-1932, but it disappeared in the summer of 1932. The twitching returned in the fall and gradually spread to the right leg and at times to the head and the right shoulder.

In the hospital forced drainage was done on two occasions, four days apart. Between 1,600 and 1,800 cc. of 0.45 per cent saline solution was injected, and from 125 to 130 cc. of cerebrospinal fluid removed. There was definite reduction in the choreiform movements after the first drainage, with further improvement after the second. Six days later the patient was allowed to go home, with instructions to remain in bed under mild medication with phenobarbital. She resumed school work after a few weeks and entered college in the fall of 1933. It is said that the twitching movements had disappeared entirely until the patient faced the extra stress of beginning college work, when slight twitching of the right hand and arm returned; this was not sufficient to interfere with her activities.

CASE 5.—In a man, aged 27 (New York Neurological Institute, Drs. Tilney and Constable), there developed in the course of a half year signs of a fairly characteristic multiple sclerosis—spastic weakness, ataxia, disturbances of coordination, irregularly distributed reflex changes, a bilateral Babinski sign and nystagmus. The spinal fluid was normal except for a slight elevation in the protein content.

Drainage was done three times in thirteen days. After an uneven response to these treatments, with a diminution of certain symptoms and intensification of others, the patient began a period of improvement which lasted about two months. Then he subjected himself to a sun cure, and coincidentally his condition retrogressed rapidly. A number of months later he returned for drainage on two occasions. Unfortunately, it has not been possible to examine him since these treatments, but from reports it seems that they have not been effective.

PRESENTATION OF CASES. DR. CLARENCE C. HARE.

CASE 1.—A woman, aged 52 (Manhattan Eye, Ear, Nose and Throat Hospital, Drs. Harmon Smith, Zabriskie, Eggston and Hare), had meningitis following right frontal sinusitis, with erosion of the posterior wall of the sinus, the sinusitis having lasted about eight years. No organisms were found in the cerebrospinal fluid by smear or culture. The meningeal symptoms had been present for one day. The temperature was 104 F.; there was sudden collapse, with hemiplegia, stupor, incontinence and rigidity of the neck. There was no evidence of infection in the blood stream; blood cultures were negative.

Before drainage the cerebrospinal fluid showed 2,500 cells, with 95 per cent polymorphonuclears; the fluid was slightly xanthochromic. Six treatments, lasting one hour each, were given in six days, from 1,000 to 1,500 cc. of 0.5 per cent saline solution being given intravenously, and from 50 to 100 cc. of spinal fluid being withdrawn. There were 275 cells, and the fluid became clearer but was still definitely xanthochromic; the polymorphonuclear cell count dropped to 40 per cent.

During the three weeks of illness the outcome was uncertain. During the period of forced drainage the temperature subsided to almost normal, although the patient remained in a semicomatose condition and could be aroused only to take fluids. The hemiplegia disappeared. In the second week of the illness the temperature was again elevated and there was a question of pneumonia, though definite pulmonary signs were not found. There were frequent sudden attacks of cyanosis, during which the condition became very critical. Lumbar punctures without intra-

venous administration of saline solution showed highly xanthochromic fluid, with 1,800 cells. Subsequent puncture showed 875 cells. The condition remained much the same except for the return of hemiplegia. The patient died suddenly about three days after the last lumbar puncture.

It was believed that the meningitis was definitely improved by forced drainage, and that death was the result more of a generalized toxemia than of meningitis. The cause of the cyanotic attacks was not determined. A diagnosis of an abscess of the brain was considered, but because of the sudden onset of the cerebral signs and the subsequent course this was discarded.

CASE 2.—A girl, aged 9 years (Drs. Zabriskie and Hare), with acute anterior poliomyelitis, for three days had shown signs of progressive injury to the cord, beginning in the arm and extending downward to include the legs and threaten the bladder and upward to produce nystagmus and impair the movements of the diaphragm.

Initial spinal punctures yielded characteristic fluid, the first fractions of which contained 182 cells, of which 84 per cent were lymphocytes; the second and third fractions showed 36 and 30 cells, respectively. On the third day after admission, forced drainage of the spinal fluid was begun with an injection of 1 liter of 0.5 per cent saline solution and the withdrawal of 90 cc. of fluid. From that time on the disease did not spread; on the following day movements in the lower extremities began to improve. Drainage was repeated on the next day, and that evening the child was less toxic and the temperature fell. After a day, a third treatment was given, and three days later a fourth. By this time the temperature was normal and meningeal signs had almost disappeared; there were improvement in the coughing reflex and improved motion of the wall of the chest, and the cell count was only 10. Following this there was general improvement in motor power, with a lessening of muscular pain and a gradual return of the reflexes to normal.

The child is now able to perform all movements required in dressing and feeding herself and in moderate exercise. There are slight atrophy of the deltoid muscles and slight muscular weakness in certain muscle groups of the lower extremities. All tendon reflexes are present, and the diaphragm moves normally. The impression is that far less extensive damage took place than the rapidly spreading initial picture made one anticipate; the residual involvement is minimal.

CASE 3.—A patient (Hackensack Hospital, Drs. Curtis, Zabriskie and Hare) who had had symptoms of acute syphilitic meningitis for four days before she was seen up to the time of treatment showed a rapidly progressive and intense meningeal reaction and an intoxication so severe that she was looked on as moribund. The removal of cerebrospinal fluid for diagnostic purposes caused no change in the clinical picture. The fluid was under high pressure, containing 156 cells, 88 per cent of which were lymphocytes. The findings otherwise were characteristic of a syphilitic meningo-encephalitic reaction.

Forced drainage was instituted on the fourth day, and two treatments were given, with an injection of 1,000 cc. of 0.5 per cent saline solution and the withdrawal of from 60 to 70 cc. of cerebrospinal fluid. The cell count dropped promptly to 23. During the course of the first drainage the patient roused from the stupor. On the following day she vomited once, and presented abdominal distention and a transient facial weakness on the left side. On the next day the treatment was repeated; four days later the temperature was normal and the meningeal signs had disappeared; two weeks later antisyphilitic therapy was resumed. Five months later the patient was well.

CASE 4.—A child, aged 13 years (Manhattan Eye, Ear, Nose and Throat Hospital, Drs. Allan and Hare), for about one month had had meningitis due to Streptococcus haemolyticus following mastoidectomy. The duration of the meningeal symptoms was one day. The temperature was 105 F.; there were headache, rigidity of the neck and a sterile blood culture. The cerebrospinal fluid before drainage contained 3,900 cells, with 95 per cent polymorphonuclears, and a smear and culture were positive.

Forced drainage was carried out five times, each drainage lasting one hour, from 1,000 to 1,500 cc. of 0.5 per cent saline solution being injected and from 59 to 100 cc. of spinal fluid withdrawn. The cell count dropped to 32, with 15 per cent polymorphonuclears; the smear and culture became negative. The temperature became normal; the symptoms disappeared, and no signs of further meningitis developed up to the twelfth day after the onset of meningeal symptoms.

CASE 5.—A child, aged 15 years (St. Vincent's Hospital, Staten Island, Drs. Cott and Hare), had meningitis due to Streptococcus haemolyticus following mastoidectomy on the right side for an infection of the ear that had lasted two days. The duration of the meningeal symptoms was one day. There were fever, delirium, headaches and rigidity of the neck; cultures of the blood were sterile. Before drainage the cerebrospinal fluid contained 19,000 cells; a smear and culture were positive.

Drainage was done fourteen times, each drainage lasting one hour, 1,000 cc. of 0.5 per cent saline solution being injected and from 100 to 130 cc. of spinal fluid withdrawn. The number of cells dropped to 34; smears and culture became negative. Marked improvement set in; the temperature became normal; headache and meningeal signs disappeared, and the patient remains well three and a half weeks later. He has been out of bed without return of symptoms.

CASE 6.—A patient, aged 33 (Holy Name Hospital, Drs. Kennedy, Tennis and Hare), had pneumococcic (untyped) meningitis following, first, otitis media complicated by labyrinthitis and, second, mastoiditis with mastoidectomy. The duration of the meningeal symptoms was one day. The clinical symptoms were: rapidly increasing meningeal signs, with a temperature of 105 F.; cultures of the blood were negative. Before drainage the cerebrospinal fluid showed increased pressure, 4,200 cells, of which 98 per cent were polymorphonuclears, and pneumococcic in smear and culture.

Conservative forced drainage was done six times, each drainage lasting one hour, with the injection of from 250 to 1,000 cc. of 0.5 per cent saline solution and the withdrawal of between 55 and 110 cc. of cerebrospinal fluid. During this period the number of cells in the cerebrospinal fluid dropped to 200 per cubic millimeter, and organisms could no longer be demonstrated in the smear. Whether they disappeared from the culture or not is not clear. Despite the alteration in the cerebrospinal fluid, the temperature remained elevated and the meningeal signs persisted. The patient died six days after the operation and six days after the first drainage. There was no autopsy.

The results in this case should be contrasted with those in a comparable case in which much more intensive forced drainage was employed. Details of the second case will be reported later.

CASE 7.—The patient, aged 23 (Drs. Haskin and Hare, Manhattan Eye, Ear, Nose and Throat Hospital), had a cerebellar abscess on the right side following an infection of and operation on the right mastoid. This case is cited only as a warning of the most serious danger which this procedure entails—the danger of pouring fluid into a lesion from which it cannot escape. Because of a mistake in diagnosis, the symptoms and signs of a cerebellar abscess were misinterpreted as indicating an oncoming meningitis. The patient was treated by forced drainage; after the sudden and rapid release of a large amount of cerebrospinal fluid, about 200 cc. of 0.5 per cent saline solution was given intravenously. Three hours later the patient died from respiratory failure; at autopsy a cerebellar abscess was found containing fluid under distinctly increased pressure, which had obviously obstructed the aqueduct by downward pressure, causing probable herniation through the foramen magnum.

CASE 8.—A patient, aged 8 years (Manhattan Eye, Ear, Nose and Throat Hospital, Drs. Cunning and Hare), had an intense meningeal reaction (meningitis?), possibly complicated by cerebral or epidural abscess, following repeated operation on the mastoid. The duration of the infection of the ear was three years. The illness followed pneumonia, the causative agent of which was uncertain. The duration of the meningeal symptoms was one week. The clinical symptoms were:

typical meningeal signs and symptoms, with progressive fever, headache and stupor. No infection of the blood stream was demonstrated. During the first week of meningeal symptoms the spinal fluid was clear, but coagulated rapidly. With the rapid increase of meningeal symptoms the spinal fluid became turbid, was under increased pressure and contained 1,600 cells, of which 60 per cent were polymorphonuclears; the content of globulin and albumin was increased. A culture was sterile.

Forced drainage was done twenty times, each drainage lasting from thirty to sixty minutes. The fluid given was by mouth and by nasal tube; none was administered intravenously. From 30 to 60 cc. of spinal fluid was recovered each time. The cell count dropped to 28; the amounts of globulin and protein became normal, and the culture remained sterile. There was gradual disappearance of all meningeal signs and symptoms; a moderate degree of sensory and motor aphasia persisted. Following the sudden discharge of a large amount of purulent material through the mastoid the wound healed. The child has remained well for eight months following discharge from the hospital.

CASE 9.—The patient, aged 22 (Manhattan Eye, Ear, Nose and Throat Hospital, Drs. Page and Hare), had an intense meningeal reaction (meningitis?) following otitis media, mastoiditis and labyrinthitis. Mastoidectomy and labyrinthectomy were performed after the onset of the meningitis. Organisms were not found. The duration of the aural infection was twelve years, with an acute exacerbation for one week. The meningeal symptoms had been present for four days. Superimposed on the symptoms of mastoiditis and labyrinthitis were signs of increasing intracranial pressure. There was no evidence of infection of the blood stream. The initial puncture before operation yielded a cloudy cerebrospinal fluid under increased pressure, with 770 cells, of which 60 per cent were polymorphonuclears. Four days later, after a period of temporary improvement following operation, the fluid was still cloudy, but the number of cells had dropped to 275; cultures remained sterile.

The symptoms were increasing when forced drainage was carried out five times, each drainage being of one hour's duration. About 1,000 cc. of 0.5 per cent saline solution was given intravenously, and from 80 to 100 cc. of cerebrospinal fluid was recovered each time. At the time of the first treatment the first fractions of fluid contained 950 cells, of which 85 per cent were polymorphonuclears; during the drainage the count dropped to 360 cells. On subsequent drainages the cell count varied up to 1,800, but smears and cultures never yielded bacteria. At the final drainage the cell count had dropped to 100, with diminution in the excess of globulin and protein.

During the course of the treatment and the succeeding days, the patient went through stormy periods, with transient paralyses, etc. Twelve days after operation and six days after the termination of the series of treatments, the temperature had dropped to 100 F., almost all focal signs had disappeared, and the patient was conscious and oriented. This improvement continued and now, eight months after discharge from the hospital, he remains well.

PRESENTATION OF CASES. DR. ROBERT W. LAIDLAW.

CASE 1.—A girl, aged 15 years (New York Neurological Institute, second division), had chorea of extreme intensity, which had come on two months after a severe illness which was called "flu" and one month before admission. Whether this was a typical Sydenham chorea or a choreiform type of acute encephalitis it is impossible to say.

Three days after admission the first forced drainage was done. In the three days it had been impossible to understand a word the patient said and almost impossible to feed her or keep her in bed; because of the incessant thrashing motions she was bruised, exhausted and sleepless. Moreover, ordinary doses of sodium amytal, scopolamine hydrobromide and sodium salicylate had had little or no effect. Seven and one-half grains (0.49 Gm.) of sodium amytal, given intra-

muscularly, resulted in twelve hours of sleep; on the following day the movements gradually returned to their former intensity.

It was after this that drainage was undertaken, under the influence of morphine, ⅛ grain (0.008 Gm), and sodium amytal, 3 grains (0.195 Gm.). In one hour and a half 1,550 cc. of 0.5 per cent saline solution was given and 120 cc. of cerebrospinal fluid was drained. During the procedure the patient slept. She wakened suddenly with an explosive movement of the entire trunk and extremities, so that the needle was jerked out of the left arm. Because of the danger of breaking or bending the needle in the back, this was rapidly withdrawn and the treatment terminated. Seven and one-half grains of sodium amytal was given intramuscularly. A few moments later the patient went to sleep and slept throughout the night. On the following morning she was quiet; the choreiform movements were mild, and speech was clearly intelligible. The improvement continued steadily throughout the day; although she was quiet that night, another large dose of sodium amytal (7½ grains) was given.

Two days later mild choreiform movements were present; forced drainage, of three hours' duration, was done, 3,000 cc. of saline solution being given and 180 cc. of cerebrospinal fluid withdrawn. Morphine ⅛ grain, and sodium amytal, 3½ grains (0.227 Gm.), were given before and during the drainage. The patient suffered from slight headache and nausea during the procedure. After this treatment the patient continued to show steady improvement; three days later it was almost impossible to see any choreiform movements of the larger joints, of the distal portions of the extremities or of the face, eyes or tongue.

In considering the relative value of the sodium amytal and of the drainage it should be borne in mind that the drug produced only transitory amelioration of the symptoms, that no amytal was administered after the second drainage, and that nevertheless from this time on the progress continued steadily. The patient remains free from symptoms after almost a year.

Case 2.—A girl, aged 12 years (New York Neurological Institute, fourth division), had typical acute Sydenham's chorea; the case is reported because after six weeks of fairly intense choreiform movement and after failing to respond to a short preliminary period of rest and medication with phenobarbital and bromide, the patient improved definitely after drainage on two occasions.

The drainage included the injection of 2,000 and 2,300 cc. of 0.45 per cent saline solution in about two hours, with the removal of 110 and 125 cc. of cerebrospinal fluid. During the treatment the patient experienced slight headache and nausea, and during the second treatment vomited once. Because of this and despite the definite decrease in choreiform movements, on which the patient herself commented, she refused further treatment. The further course cannot be interpreted because of the introduction of other methods of therapy.

Case 3.—A boy, aged 7 years, with probable acute encephalitis, though the diagnosis was not established with certainty, shortly after a mild infection of the upper respiratory tract, not associated with evidences of involvement of the central nervous system, became drowsy, irritable and subject to nightmares. There were also headache and a tendency to fall to the knees without loss of consciousness. Repeated neurologic examinations revealed equivocal signs, with scattered differences in reflexes and varying observations as to the plantar responses. There were a fine lateral nystagmus and a ticlike protrusion and retraction of the tongue.

One treatment by forced drainage was given; it resulted in marked temporary amelioration of all symptoms. Because of the uncertain diagnosis and the uncertain findings, the treatment was not repeated. It is reported that since discharge there has been a return of drowsiness, but without the original irritability. The spinal fluid was at no time abnormal.

It may be that repeated drainages would have acted prophylactically in this case.

Case 4.—A man, aged 60 (New York Neurological Institute, fourth division), with a history of an early syphilitic infection, experienced transitory episodes of paresthesias in the extremities. In a year or so certain motor disturbances gradually appeared, e. g., cramps, drawing sensations and weakness. A few months

later the patient became depressed and retarded. The attacks recurred frequently and with increasing severity. There were generalized spasticity, slight hemiparesis on the right side, equivocal plantar responses, unequal pupils, one of which was sluggish to light, facial weakness in the center of the right side, some degree of aphasia, and a rapidly progressive parkinsonian picture. The Wassermann reaction of the blood was negative for crude antigen, and 1 plus for cholesterolized antigen. The spinal fluid contained 26 cells, of which 96 per cent were lymphocytes, with increased globulin, 81 mg. of protein, a colloidal gold curve of 3322221100 and a 4 plus Wassermann reaction.

Rather drastic drainage was done four times within a month, with the injection of from 2,000 to 3,000 cc. of 0.3 per cent saline solution and the removal of 140 cc. or more of cerebrospinal fluid. In two treatments silver arsphenamine was added to the fluid injected. At the end of that time not only had the rapid progress of the condition ceased, but improvement was satisfactory. The difficulty in speech had disappeared; the parkinsonian facies and posture had improved; the right facial weakness was less marked, and power in the right side of the body was definitely better.

After a period of routine antisyphilitic treatment the patient was readmitted, three months later, for another series of treatments by forced drainage. In the interval, the condition had remained unchanged. The spinal fluid contained 32 cells, of which 98 per cent were lymphocytes, globulin (3 plus) and 384 mg. of protein. At the conclusion of two thorough drainages the fluid contained only 2 cells, a smaller amount of globulin (1 plus) and 57 mg. of protein. The colloidal gold curve was 1111100000, and the Wassermann reaction remained 4 plus.

Six months later, the patient was admitted to the hospital for the third time, having received intensive antisyphilitic treatment since the previous discharge. The condition had not grown worse; the patient had noticed general alleviation of all symptoms, except perhaps for mild weakness of the legs. There was slight relative overactivity of the deep reflexes on the right, with slight spastic dragging of the foot and an uncertain plantar response. Two treatments were given, consisting of the injection of from 1,500 to 2,000 cc. of 0.45 per cent saline solution on one occasion, with the addition of 0.3 Gm. of silver arsphenamine at the end of the injection. Between 140 and 170 cc. of cerebrospinal fluid was withdrawn. The patient continues to receive antisyphilitic therapy, and the condition has shown no further progress.

This case of meningovascular syphilis is of interest in that the treatment consisted of a combination of forced drainage with specific antisyphilitic therapy. This combination not only succeeded in checking the initial rapidly advancing progress of the disease but brought about a slow but definite improvement.

General Comment. Dr. Lawrence S. Kubie.

My associates and I are aware that we have too few cases in any one group—except perhaps that of acute Sydenham's chorea—to say how valuable the method will prove to be from a therapeutic point of view. We have proceeded conservatively, and have used the method only when it was understood by the patient and by members of the family that we could not promise therapeutic results and could say only that we were reasonably sure of not doing any harm. Many patients have refused treatment, and we have undertaken treatment in situations in which we could not hope for much result. We have not observed that the treatment has done any harm, with the possible exception of a young woman with multiple sclerosis in whom disturbances of the bladder were more severe for several months after the treatment than before.

Symptoms and signs, which in some cases have been of long duration, have been profoundly modified after the treatment. At times this has occurred when it seemed that there could no longer be any remaining active inflammatory process. This seems to indicate that there may be persistent but reversible changes the pathologic basis of which is by no means clear, but which can at times respond well to this procedure. We are not yet in a position to make any generalization

as to a standard optimal method of administering the treatment. There are serious technical difficulties, and it has not been possible to push our experimental work further in this direction.

A few patients have been treated at other places by impartial and careful observers who have been kind enough to let me know of their results. The patient presenting the most striking example was a man with pneumococcic (type III) meningitis treated at the Strong Memorial Hospital in Rochester, N. Y. He had typical meningitis, which originated with mastoiditis and a cholesteatoma. He was admitted to the hospital on the fourth or fifth day of the meningeal symptoms, and a radical mastoidectomy was performed by Dr. Clyde Heatley. At that time the fluid contained 2,000 cells, with abundant organisms; but cultures of the blood were persistently negative. The patient was placed on a Bradford frame and subjected to continuous drainage of spinal fluid for several days, accompanied by the administration of large quantities of fluid, both intravenously and by mouth. There was free and abundant drainage throughout the entire time. In a short time the fluid became sterile, the cell count fell rapidly and the signs diminished. At the end of a week, drainage was discontinued, except for periodic lumbar punctures. The rapid improvement continued, and the patient was discharged a few weeks after the onset. Convalescence at home was interrupted by a relapse, in which there were fever, recurrence of meningeal signs and palsy of the sixth nerve on one side. The patient was readmitted to the hospital, and the spinal fluid was drained again for several days. The wound was opened, and a small cholesteatoma, which had been overlooked at the first operation, was removed. Under forced drainage improvement was again rapid, and in a short time the patient was discharged; he has remained well since.

Dr. T. H. Cheavens, of Dallas, Texas, wrote to me of one case of chronic encephalitis with a parkinsonian syndrome in which there was no response to treatment, of two cases of meningovascular syphilis in which improvement occurred and of two cases of pneumococcic meningitis, in both of which death ensued, although one patient seemed to improve temporarily. In addition, he had treated two patients with tabes, one in the very advanced stage and the other in the moderately advanced stage. The patient with the severe case showed marked improvement in gait and in the general condition. The other patient was subjected to drainage twice before antisyphilitic therapy was given. Gait improved markedly, pains disappeared, and after five drainages combined with antisyphilitic treatment the patient can walk without a cane and can stand with the eyes closed; libido has returned, with nocturnal emissions, and control of the bladder has improved. This is comparable to some experiences that Dr. Retan has had in Syracuse. Dr. Retan has had encouraging results, especially in a group of about a dozen acute cases of Sydenham's chorea, and in a small group of cases of poliomyelitis.

Dr. Brickner referred to me a patient with severe multiple sclerosis because she was hypersensitive to all forms of quinine. This patient was so ill that the treatment was undertaken reluctantly. Many of the symptoms were of several years' duration, and for a year and a half the disease had been progressing rapidly and intensively. In March 1933, one conservative drainage was done, without marked changes except the disappearance of one or two recent symptoms. This is in line with our general experience—namely, that in multiple sclerosis the acute symptoms tend to melt away with extraordinary rapidity after the first or second drainage. No further treatment was given until June, when intensive drainage was done five times, each drainage lasting between four and six hours, with the administration of from 3,000 to 4,000 cc. of 0.45 per cent saline solution and the collection of between 200 and 300 cc. of cerebrospinal fluid. The patient was reexamined in July. She looked well and said that she had improved in various ways. The arms and legs were steadier. She could walk a little without a cane. Her voice was stronger and easier, so much so that it was not always recognized by friends over the telephone. Her writing showed remarkable improvement. Memory was better. Vision, as tested by an impartial ophthalmologist, had improved from 15/70 to 15/40 in the right eye, and from 15/200 to 15/100 in the left eye; there was some

recovery of color vision in the left eye, which had previously been totally deficient in this respect. These subjective and objective improvements were confirmed by Dr. Brickner in an independent examination of the patient. Unfortunately, through the summer, however, the patient was subjected to severe emotional stress, and had at least one severe fall from the porch of her home to the ground below. In September, the condition began to retrogress. Drainage was done three times, much the same as the drainage which had been given in June. There was no immediate alleviation of the condition, although the retrogressive tendencies seemed to cease. Gradually, during the fall and winter, the patient began to improve, and with a partial resolution of some emotional problems a period of improvement seemed to set in. Whether this had anything to do with the treatment is, of course, impossible to say. It is of interest to note the apparent quick response to the first series of treatments, and the doubtful, limited or delayed response to the second. At present the patient has been desensitized to quinine, and the value of this form of therapy is again being tested; this complicates any further interpretation of the case.

There is no field of study more deceptive than research in therapeutic procedure. Eagerness to see results is likely to mislead one into overestimating the value of treatment in successful cases and, conversely, to find excuses for failures. I have not tried to push the method blindly. There are certain disadvantages in this, in that in some instances the method is applied so timidly that it can hardly be said to be given a fair trial. Fundamentally different procedures have been used by others and have been called by the same name. For instance, one pediatrician told me of using hypertonic saline solution in association with lumbar drainage, an attack so fundamentally different in its physiologic effect as not to be comparable with this procedure. I am particularly eager to see the method tried more extensively in cases of infections of the meninges which are secondary to involvement of the bone of the middle ear, the mastoid, the labyrinth and the sinuses. It may be found, however, that it is necessary to proceed in several stages here, perhaps first treating the meningitis before subjecting the patient to the more radical operation of labyrinthectomy. In such cases it seems logical to attempt first to reduce the meningitis and cerebritis by forced drainage, then to eliminate the focus in the bone, and at the same time to continue drainage throughout the operation and to follow the operation by a prolonged period of drainage. It is possible that a certain number of these desperately ill patients may be saved by such a treatment.

In the group of pyogenic infections it is of great importance to keep in mind the experience of Weed and Wegefarth, which has recently been confirmed in experiments conducted in the laboratory of Rich in the department of pathology of the Johns Hopkins Hospital. These investigators found that infection of the blood stream can be carried over into the meninges by drainage of the cerebrospinal fluid. If this is true, it raises a question as to the advisability of using forced drainage in the presence of bacteremia. This may account for the fact that all of the patients with pyogenic infection who died, both among Dr. Hare's patients and in the group whom I have treated personally, have been patients in whom an overwhelming infection of the blood stream existed before the treatment was begun. This may mean only that there is such a profound generalized infection that the treatment of the meningitis alone is not sufficient to save the patient's life. Only by prolonged experience will one be able to settle the question of the significance of invasion of the blood stream as a contraindication to the method.

DISCUSSION

Dr. George H. Hyslop: In one of his essays Osler set forth as guiding principles in clinical research the methods of the dominant school of French physicians in the period beginning about 1820. He was much influenced by the importance of proper statistical methods. The material which Dr. Kubie and his associates has presented should be subjected to the rules by which Osler was influenced. I think that it will be ten years at least before it is known whether this procedure is of real value.

DR. LEON H. CORNWALL: I wish to comment on my experience with this method of therapy. I cannot state with certainty in how many cases I have employed it; they are certainly not less than ten and may possibly be twenty. They include syphilis of the central nervous system, serous meningitis, pneumococcic meningitis, streptococcic meningitis and multiple sclerosis. I have not seen any beneficial result in multiple sclerosis. The number of cases of purulent meningitis has been small, not more than four, and they terminated fatally. I do not know whether there were positive blood cultures in any or all of them. In the cases of neurosyphilis, forced drainage was used in conjunction with other types of therapy; therefore I doubt whether they could furnish any evidence to substantiate the efficacy of this type of therapy.

I agree with Dr. Kubie and Dr. Hyslop that time alone will warrant final conclusions. I believe that the rationale of forced drainage is based on sound physiologic principles. The method deserves more extensive trial in order that a large number of cases may be submitted to critical analysis. In the case of purulent meningitis I believe that continuous drainage is to be recommended, for it seems to give hope for a more favorable outcome than one ordinarily sees. In neurosyphilis, I believe that forced drainage should be combined with the arsenicals and with hyperthermia.

By a simple arrangement of apparatus, sodium amytal can be given intravenously immediately before the institution of forced drainage. When that is done it has been my experience that the patient passes into a somnolent state and is unaware of the treatment during the period of an hour or more.

DR. RICHARD M. BRICKNER: I had two years of experience with one of Dr. Kubie's patients with multiple sclerosis before forced drainage was done. Various means were attempted to give her quinine, but she was never able to take it except in minute doses. She was not one of those patients who always respond dramatically to each new form of treatment. At the time when the first drainage was done she could hardly walk with a cane; her handwriting was reaching the stage of illegibility, and her eyesight was diminishing rapidly. All of these symptoms improved strikingly after the drainage. It is true that the improvement did not last indefinitely and that later there was another slump, but there is no doubt that the abrupt change was associated with the drainage.

I wish to raise one general question, but specifically in relation to Sydenham's chorea. Is fever sometimes associated with the treatment, and did fever occur in the cases of chorea in which the treatment was successful? This is important in view of recent work which shows that chorea may respond well to fever therapy.

DR. BERNARD SACHS: As I listened to these case histories the question arose in my mind whether the improvement occurred because of the drainage or in spite of it. One should be careful before any such radical procedure as this is given endorsement as a routine method of treatment. I can understand that there is a sufficient rational basis for it in distinctly infectious cases, and in cases in which there is reason to believe there is a marked increase in the cerebrospinal fluid. Do not look on the cerebrospinal fluid as more or less superfluous. It is not. The entire nervous system, especially the spinal cord, demands this cushion, and as much of it as possible, so that anything which is akin to desiccation of the spinal cord is a matter which should be regarded seriously. Why this treatment should be especially recommended in cases of disseminated sclerosis I cannot see; I doubt whether there is sufficient evidence of an increase in the cerebrospinal fluid in disseminated sclerosis, and I do not think that the larger number of cases of disseminated sclerosis are clearly of an infectious origin.

Cases of cerebrospinal syphilis in which treatment is given by forced drainage together with arsphenamine and other antisyphilitic drugs prove nothing as to the value of forced drainage. To prove the value of a method of this sort it must not be combined with any other form of treatment.

Forced drainage may prove to be useful in the earlier stages of distinctly infectious disease of the cerebrospinal system, and no doubt particularly so in cases in which the condition is inclined to become purulent. The danger of the method

is well illustrated in the case of abscess in the cerebellum. From long experience, I cannot repeat often enough that even lumbar puncture is not wholly innocuous. Before resorting to forced drainage one should make sure that there is no abscess or tumor of the cerebellum, because a fatal outcome from the sudden change in intracranial pressure is almost certain. While I have been much interested I wish to make a plea for the careful consideration of the merits of forced drainage, and to urge that it not be given endorsement as a safe and routine method of treatment until there is a great deal more evidence regarding it.

DR. LAWRENCE S. KUBIE: To answer Dr. Brickner's question, as far as I know, my associates and I have never encountered fever during or after treatment, even when we used salt solution of such low concentration that we looked for a certain amount of hemolysis. Therefore, the favorable results in chorea are not due to the effect of nonspecific fever therapy.

With regard to the conservatism of the others who have discussed this subject, we assure them of our almost complete agreement with their point of view. No conclusions are possible without a long period of observation and without careful comparative statistical data on treated and untreated patients. This is particularly true with regard to the infectious diseases of the central nervous system, since these run such extraordinarily variable courses. We must also agree that it is difficult to draw conclusions if one has used more than one form of treatment. Nevertheless, here one meets a human problem which is in conflict with the interests of pure research. In the case of syphilis, for instance, certain antisyphilitic measures have value, even though their value in certain directions is limited; therefore, it seemed to us that we should add our new attack to the old one, rather than discard the older while testing out the newer. We stated that these cases were not advanced as proving anything, although in certain instances drainage and the apparent results from it preceded the use of antisyphilitic measures.

The third point raised in criticism has been with regard to our choice of material on which to test the method. There is no question as to what our preference would be if we could get all the material that we want. We should choose infections of the nervous system, either pyogenic or virogenic, and we should try to see the patients as early as possible. It is always true, however, that a new method is tried in cases only when the condition is advanced or even when the patient is moribund. Frequently, therefore, favorable chances to try out the method are lost. Contrariwise, with any new method one is constantly being subjected to the temptation to try it on a great number of heterogeneous disorders on the chance that it may prove useful. Physicians have tried to induce me to use this treatment even in degenerative diseases of the nervous system; naturally one refuses such invitations. With regard to the special case of multiple sclerosis, however, it did not seem to be of primary importance whether it was on an infectious basis or not. We know that the inflammatory part of the process is important in producing symptoms, and it seemed that forced drainage might ameliorate that part of the condition which was due to inflammation. Our hopes and expectations with regard to multiple sclerosis are limited to this notion: that since the recent symptoms of an acute exacerbation seem to melt away under the influence of forced drainage, its early and repeated use with every fresh outbreak of the disease ought to diminish the amount of permanent structural damage which each exacerbation produces and therefore should, logically at least, decrease materially the cumulative disability which gradually overtakes these patients. It is unnecessary to say how difficult it will be and how long a time it will take to prove the truth of any such expectations.

I wish to clear up one misunderstanding, contained in a comment of Dr. Sachs. There is no need to look for an increase in the cerebrospinal fluid as a prerequisite for attempting this procedure. The fundamental difference between forced drainage and simple spinal drainage is that in simple drainage there occurs a collapse of the leptomeninges around the central axis of the central nervous system, which obstructs further drainage as soon as the preformed lake of cerebrospinal fluid has been evacuated. In forced drainage, on the contrary, because of the changes

induced in the osmotic pressure of the blood stream, a new accumulation of cerebrospinal fluid occurs continuously to replace the fluid that is being withdrawn, so that no such collapse of the meninges occurs and free pathways of drainage are maintained throughout. This method is more than a mere release of pressure, more than a mere evacuation of the superficial lake of preformed fluid; it is a true perineuronal and perivascular drainage.

In conclusion, I want to stress the fact that we do not look on forced drainage as the exclusive panacea for all infections and inflammations of the central nervous system. It does not prevent the use of specific pharmacologic or immunologic agents as these develop, but is a sound physiologic aid to their effectiveness.

TUMORS OF THE THIRD VENTRICLE. DR. MOSES KESCHNER and DR. NATHAN SAVITSKY (by invitation).

In spite of numerous attempts to establish a syndrome for tumors of the third ventricle, their diagnosis still presents great difficulties. Six verified cases of tumors in this region are presented.

CASE 1.—Before the patient was subjected to encephalography, the clinical diagnosis rested between a tumor in the left cerebral hemisphere and a subdural hematoma. The findings were those of a tumor of the third ventricle. An ependymal cyst within the third ventricle was found at operation and was extirpated. The patient made a complete recovery.

CASE 2.—The clinical diagnosis in this case rested between a pituitary tumor and a growth in the right cerebral hemisphere. Exploration failed to reveal a tumor. The patient was subjected to roentgenography following the injection of air and the picture was interpreted incorrectly. At necropsy a small medulloblastoma was found projecting from the posterior wall of the left side of the third ventricle at its junction with the aqueduct. Reexamination of the picture following necropsy showed that had the former film been correctly interpreted the proper localization could have been made prior to the exploration.

CASE 3.—A clinical diagnosis of a right frontotemporal neoplasm was made before ventriculography was done. Neurofibromatosis was suggested because of the presence of pigmented moles on the skin in various parts. Exploration did not reveal a tumor. Ventriculography carried out after the exploration pointed to the presence of a tumor in the region of the third ventricle. Signs of multiplicity were noted afterward. This suggested the diagnosis of tuberous sclerosis. Necropsy revealed the presence of a central neurinoma in the form of a hard mass, about 2 cm. in diameter, invading the anterior portion of the third ventricle. Small, hard nodules of tuberous sclerosis were found in other parts of the brain.

CASE 4.—The patient showed a hypopituitary syndrome of twelve years' duration with marked hypothermia, diabetes insipidus and somnolence. There were many nevi over the chest. Bilateral primary atrophy of the optic nerve and bilateral constriction of the fields for color and form were present, with a normal sella on roentgenographic examination. At necropsy an angioma was found at the base of the brain. This tumor invaded the floor of the third ventricle.

CASE 5.—Before ventriculograms were made the clinical diagnoses were frontal tumor on the right side, parasagittal neoplasm, chronic degenerative disease of the nervous system and chronic encephalitis. Ventriculograms showed the presence of a tumor in the region of the third ventricle. At necropsy a craniopharyngioma was found pushing up and almost obliterating the third ventricle. This tumor extended as far back as the region of the aqueduct and invaded the cerebral peduncles.

CASE 6.—The clinical diagnosis was tumor of the posterior fossa, probably a cerebellar neoplasm. No air studies were made. Suboccipital exploration gave negative results. No vegetative disturbances were noted. At necropsy a soft tumor was found at the base of the brain. This tumor compressed the third ventricle and destroyed its floor and the infundibular region. The microscopic diagnosis has been deferred pending further histologic studies.

The clinical diagnosis of a tumor of the third ventricle is unusually difficult without air studies. While the early onset of vegetative disturbances is important evidence that the tumor is in the region of the third ventricle, the absence of such clinical signs does not always exclude involvement of the hypothalamic region.

Air studies, properly performed and interpreted, should be utilized more frequently as an aid in the localization of tumors of the brain. Unless the localization of the tumor is beyond doubt, no exploration should be attempted without air studies. Careful attention should be paid to the third ventricle in the interpretation of the film.

The following abnormalities in the picture point to the localization of the tumor in the region of the third ventricle: There may be failure of visualization of the third ventricle with adequate filling and more or less uniform dilatation of both lateral ventricles. A deformity of the third ventricle may sometimes delineate the tumor; at other times the third ventricle may appear only partially filled with air. In the presence of dilated lateral ventricles and a deformed third ventricle, absence of air in the aqueduct, fourth ventricle and basilar cisterns is indicative of a tumor in the posterior portion of the third ventricle (only with ventriculography). Dilatation of the third ventricle without deformity may be seen in the anteroposterior view when the tumor is located in the posterior portion of the third ventricle.

DISCUSSION

DR. IRA COHEN: Drs. Keschner and Savitsky have clearly shown that there is no such thing as a distinct syndrome of tumor of the third ventricle. If there are bouts of headache with change in posture in a patient with papilledema without any localizing signs, one may suspect the presence of an intraventricular tumor. I agree that that air studies properly carried out and interpreted are essential. However, the interpretation of even good ventriculograms is not always simple. Not only are ventriculograms necessary for diagnosis, but if one is to accomplish anything, a good ventriculogram will be of service to the surgeon in showing the method of approach, whether it is through a dilated lateral ventricle into the third ventricle for an anteriorly placed tumor, or possibly transcallosally in the case of a tumor of the posterior part of the third ventricle.

If one were to draw conclusions from the cases reported this evening, one would think, with the exception of case 1, that there was no such thing as a surgical procedure for tumor of the third ventricle. There is, as in case 1, a type of tumor which lies completely and wholly within the third ventricle. It may be a cystic or a solid growth, and it is in this type of case that operation offers something. Dr. Stookey has reported two cases of cystic type. Dr. Dandy has reported twenty-one cases with fourteen recoveries.

DR. LEO DAVIDOFF: It is obvious that the authors of the paper were struggling with the difficulty of what they were to include under the title of "Tumors of the Third Ventricle," and what to leave out; that problem has been a continuous one in all that has ever been written on the subject. If one were to stretch the point, one might perhaps consider the pituitary adenomas which grow out of the enclosure of the sella turcica and encroach on the walls of the third ventricle as belonging in this category. In the same way the suprasellar meningiomas that compress the anterior wall of the third ventricle might be so included. The craniopharyngiomas not only compress the wall but compress it so completely that often nothing is left of it, so that they might also be included among tumors of the third ventricle. It may justly be said, therefore, that the material presented this evening is not uniform in that some of the tumors are in the third ventricle and others in the wall. At the same time, the authors have clarified the situation. In the strictest sense, perhaps the only true tumor of the third ventricle described was that in case 1, and in this case clinical symptomatology was characteristically sparse. The chief symptoms were those of an increase in intracranial pressure, but in retrospect the characteristic thing about this increased pressure was its intermittent character. The ophthalmologist observed an elevation of the optic disk from practically nothing to 3 diopters within twenty-four hours, and a recession took place with

equal speed. Moreover, as one went back to the history, it was possible to elicit the fact that the headaches became worse when the patient bent over books; for relief, he would lie down on a bed with the head thrown back, whereupon the headaches disappeared. This type of reaction is easy to understand if one conceives of the tumor as acting like a ball valve. Indeed, these cases are sometimes reported by coroners as those of apparently perfectly healthy persons who die suddenly on the street. As a rule heart disease is thought to be the cause of death, but at postmortem examination the heart is found to be normal and one observes a tumor in the third ventricle which has suddenly blocked the cerebrospinal fluid pathways.

At the New York Neurological Institute, we have had five instances of such a cystic tumor blocking the foramen of Monro. In each case an operation was performed. The first patient died, perhaps as a result of our inexperience with this type of operation; the others have recovered and are well.

Dr. Cornelius G. Dyke: There is often strong evidence that a tumor is present in the third ventricle; at the New York Neurological Institute, as Dr. Davidoff has said, we have had five such cases in four of which operation has been performed. From the roentgenologic point of view, I should emphasize that every bit of evidence in a film must be utilized in order to make the diagnosis. Frequently in ordinary films of the skull (without the injection of air) evidence of a generalized increase in intracranial pressure is present which points to an intracranial tumor. In two of our cases the pineal body, in the ordinary films, was displaced posteriorly and downward, indicating that the tumor was in the anterior portion of the intracranial cavity.

Either encephalograms or ventriculograms may be used to establish the diagnosis. In the interpretation of films in a case in which tumor of the third ventricle is suspected I prefer to utilize an encephalogram rather than a ventriculogram for, in my opinion, the former makes a more definite diagnosis possible. With encephalography, enough air usually seeps by the tumor into the lateral ventricles to outline them partially. Frequently some air remains in the third ventricle and is deformed by the tumor.

The roentgenologist must be content with making a diagnosis on the following points: the size, shape and position of the ventricles, localized deformities and the point at which the block occurs. The roentgenographic findings on which a diagnosis of a tumor of the third ventricle should be based are: (1) symmetrical dilatation of the lateral ventricle, (2) complete or partial filling of the third ventricle, (3) deformities of the air outline when present in the third ventricle and (4) demonstration of a block of the cerebrospinal fluid pathway by ventriculography at the foramen of Monro, and at the rostral end of the aqueduct of Sylvius by encephalography.

Dr. Nathan Savitsky: A group of tumors of the midline of the base of the brain has been presented, each of which caused a marked distortion of the third ventricle, with no shift or distortion of the lateral ventricles; none was diagnosed clinically without the aid of roentgenography following the injection of air. There is no way of making a clinical diagnosis. About eighty recorded cases of tumor of the third ventricle were studied. In cases of so-called ependymal cyst one occasionally notes that the patient obtained marked relief from the symptoms on reclining. In the particular case it has little value. While an intermittent course and relief on change of position of the head are suggestive, a definite diagnosis cannot be made without further study. Occasionally there may be relief on change in position in cases of increase in intracranial pressure due to a tumor anywhere. A patient had severe headaches for many years which were completely relieved on assuming a reclining posture. She would lie in bed for days because that position offered her marked relief. She had bilateral papilledema with no localizing signs. There were good grounds for suspecting a tumor of the third ventricle. An air study was done, but no signs of a tumor were found. An operation was performed. As far as was known there were no definite signs and symptoms of a tumor in the midline at the base of the brain distorting the third ventricle. Clinically, it makes no difference whether the tumor arises in the wall of the ventricle, in the choroid

plexus, from the glia cells in the floor of the ventricle or from the perivascular connective tissue just below the floor. None of these patients should be operated on without a correctly interpreted ventriculogram.

DIFFERENTIAL DIAGNOSTIC TYPES OF SUICIDE. DR. GREGORY ZILBOORG.

Clinical views on suicide have led to the belief in the tradition that only persons in psychotic depressions are apt to commit suicide. Suicide without a previous history of depression usually raises the question whether or not a so-called normal person ever commits suicide. Careful study of clinical material shows that depressive psychoses are not the only psychopathologic conditions which may lead to suicide. Persons with hysteria, obsessional and compulsion neuroses and schizophrenia are subject to suicidal drives which end not infrequently in death. The various theoretical views on suicide prevalent in the past century or so failed to solve the problem as to the psychic causation underlying the drive to die. As a matter of fact, for many centuries the general attitude of science and religion toward suicide has been that of admiration. Only in the course of the past fifteen hundred years has suicide been condemned, and not until about two centuries ago has it been considered as a pathologic phenomenon. Recent theories (of the past twenty-five years) of suicide have dealt mostly with depression; neither kraepelinian psychiatry nor psychoanalysis has reached a causal point of view on suicide. Setting theories aside, one may utilize the recent psychiatric and psychoanalytic contributions from an objective clinical point of view and attempt to establish objective clinical criteria that may help: (1) to foresee the possibility of suicide in a given case, even if the death drive does not happen to be as yet in evidence, and (2) to differentiate clinically the psychologic types of suicide.

Cases illustrating both points are cited, representing a variety of clinical entities. It appears that (*a*) a strong emotional attachment to the mother, combined with prolonged oral indulgence or severe weaning, presents serious predispositional factors, regardless of the formal clinical diagnosis; (*b*) persons who have identified themselves with a dead person at one of the turning points of development, like the Oedipus conflicts (between the ages of 4 to 6) or puberty, present the greatest tendency to suicide; (*c*) suicide can be understood best by a comparison of the person with the phylogenetic history of suicide. Ethnologic data may be cited to illustrate the origin of suicide among primitive races and the similarity of the psychologic mechanisms involved with those of suicide in civilized peoples today. Evidently the riddle can be solved best by a continued systematic comparative study of ethnologic and present day psychopathologic data. However, the practical clinical value of present day psychiatric knowledge is great so far as a number of prospective suicides can be recognized early and prevented.

DISCUSSION

DR. MORTIMER W. RAYNOR: The question of suicide is an outstanding psychiatric and sociologic problem. It is of interest that suicide is generally more prevalent in times of prosperity than in times of depression. From the newspapers one gets the opposite point of view. The mind of the community is directed away from the facts. It is known also that suicidal attempts follow fashion. Dr. Gregory said that whenever a patient who has taken a new drug or has made some spectacular type of suicidal attempt is admitted to Bellevue Hospital and the case is featured in the newspapers, others who have made similar attempts at suicide are seen. The fact that a patient makes one unsuccessful attempt at suicide ought to make one suspicious that he will make another. There is almost always a recurrence. The patient rarely succeeds at the first attempt, but he may on a subsequent attempt. Another point that I wish to stress as a warning signal is sudden improvement in a depressed patient. Frequently, after a patient has made up his mind to commit suicide he appears better; the tension seems to be relieved and he makes planned and serious attempts to destroy himself. That is the time when he needs the closest supervision. Depressed patients with somatic delusions are apt to have suicidal impulses.

The problem of suicide has not been studied thoroughly; one has merely begun to scratch the surface. I think that it is of great importance to look into the dynamics of the situation with the idea of discovering some of the mechanisms which lead to suicidal attempts.

DR. LAWRENCE S. KUBIE: This important problem presents many special difficulties to the student. Obviously, the first handicap is that the most successful suicides cannot be studied because of their success. One must be content to study the persons whose efforts have not attained their goal. Furthermore, to the best of one's ability one prevents suicidal patients from repeating the attempt. This adds a new difficulty. In studying neurotic behavior it is always difficult to understand it from any single manifestation. Understanding grows by meeting the symptom again and again as it repeats itself in varying situations. Suicide is a neurotic act, and a complicated one; naturally, one must try to limit its occurrence, and yet this limitation greatly complicates the problem of understanding it.

I called suicide a neurotic act on purpose, because the classic psychiatric attitude that suicide is an act which grows out of an emotional disturbance is obviously an oversimplification, which does not do justice to the truth. There are too many patients with depression who make no effort at suicide and too many patients without clearcut affective disturbances who do make such efforts to permit any such generalization to stand. If there is one contribution of psychoanalysis to psychiatry that is of dominant significance, it is the conception of the masked neurosis, the hidden neurosis that may underly either a psychosis or an apparently normal person's adjustment to life; it is an understanding of the part played by the mechanisms of the marked neurosis in the suicidal drive which will unlock the door to many obscure issues.

In this study one must come to understand the unconscious meaning of death in different kinds of neuroses and psychoses. What the fantasy of death means to a paranoid patient who leaps out of bed and hits his head on the floor cannot be the same as the unconscious fantasy of death in a depression or in a panic state. Suicide as atonement, as escape and as revenge are all different acts psychologically, even though the final element of suicide ends in extinction. There are people for whom death is always an alluring Eden, an escape from every difficulty. There are those for whom death means reunion with some one who has already gone. In each case the psychologic content demands special study. There are even instances in which suicide appears as a special manifestation of a repetition compulsion. Thus I have seen a hospitalized patient nick himself fifty times with a razor blade before he could stop. I have seen one person make three efforts at suicide, each time from a different set of conscious and unconscious psychologic motives. There are other cases, however, in which repeated efforts at suicide apparently arise from similar and recurrent motivations.

Obviously the problem is complex; one of the most interesting of Dr. Zilboorg's contributions is his study of the ethnologic background. From this attack much illumination may be expected. Dr. Zilboorg has pointed out the dangerous oversimplification of the attitude which would limit the issue of the suicidal risk to the state of psychotic depression, neglecting its occurrence in other neurotic and psychotic settings and turning one's back on it as a purely moral or custodial problem.

DR. GEORGE VAN NESS DEARBORN: Dr. Zilboorg did not have time to state his diagnostic types. I wish he had done so. I hope that he includes in that list of diagnostic types suicide committed by normal and rational adults, because I am certain that occasionally there is a certain amount of justification for suicide from the old-fashioned pessimistic point of view. I cannot agree with Dr. Kubie that there is always a neurotic taint connected with suicide. It seems to me that under certain conditions it is both logical and even morally justifiable. The life for which one did not ask one is not, ethically speaking, obligated to continue under all conditions.

DR. GREGORY ZILBOORG: With regard to the last few remarks I wish to state: Even the anatomist who deals with rigidly definite structure has abandoned of late

the search for the normal in the flesh. This abstract concept will remain abstract in biology; a perfectly normal person has not been found at autopsy; it should not be surprising, therefore, that I cannot find any psychologically normal person. As to the so-called justifiable suicide, one must remember that such appellations do not throw much light on the subject; the psychiatrist may call such cases "manic-depressive," while the psychoanalyst may dub them "oral types," but these labels will continue to mean little. The trend of thought which I endeavored to convey is this: While psychoanalysis has divorced itself from the traditional procedure of merely classifying and labeling, and while it goes deeper into the dynamics of a given psychologic problem, it has drifted a bit too far away from the clear recognition of the objective clinical picture. Yet on the basis of psychoanalytic studies it appears that a number of additional data are now brought to light which if observed could sharpen diagnostic wits and enable one to see more clearly both the nature and the meaning of the given clinical picture. My paper is only a modest attempt to make a contribution in this direction.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY AND SECTION OF DERMATOLOGY AND SYPHILIS

Joint Meeting, April 10, 1934

CLARENCE P. OBERNDORF, M.D., *Chairman, Section of Neurology and Psychiatry*

LEO SPIEGEL, M.D., *Chairman, Section of Dermatology and Syphilis*

PSYCHOGENIC ASPECTS OF DISEASES OF THE SKIN. Presented by DR. JOSEPH V. KLAUDER, Philadelphia.

In describing the psychogenic aspects of diseases of the skin the following phases must be considered: the influence of the skin on the psyche, the influence of the psyche on the skin and the clinical aspects of the relation of the psychologic phenomena to diseases of the skin.

The Influence of the Skin on the Psyche.—One is more conscious of the skin than of any other organ. It occupies an important place in the consciousness, not alone as an abstract idea, but because it is the site of many sensations. Frequently an insignificant blemish, mild acne, a few superfluous hairs or, indeed, any mild abnormality of the skin produces a psychic reaction; it decreases the self-respect of the patient and produces a feeling of inferiority, of abnormality or of uncleanliness that is difficult to overcome.

The basis of the psychic reactions which cause a sense of inferiority, of abnormality or of uncleanliness must be considered. Any striking deviation from the normal in the face or the form is likely to influence one's fate. The fear and the dread of disfigurement are innate in mankind. That this was true in biblical times may be surmised from the admonition in the third book of Moses, which forbids one who has a blemish or is lame, deformed or blind to enter the temple to offer the bread of his God.

The conception of a connection between bodily beauty and psychic perfection is apparent in the history of the beginning of the science of psychognomics. The influence of the decoration of the skin, of the adornment of the human body and of clothes on the ego may be correlated with the influence of the appearance of the skin on the consciousness and with the effect of cutaneous involvement on the ego.

The Influence of the Psyche on the Skin.—The psyche exerts a greater influence on the skin than on any other organ. This influence is apparent in the many cutaneous expressions of the emotions. The skin is an important organ of expression, comparable only to the eye.

Suggestion in hypnosis can produce such cutaneous lesions as erythema, vesicles, bullae, lesions resembling burns, ecchymosis and bloody exudate from a previous dermatographism. Sympathetic pain and cutaneous lesions have been reported as occurring immediately following the sight of suffering or accident, for instance, the production of an ecchymosis as a result of seeing a friend bleed.

The physiology of the skin is intimately related to the sympathetic nervous system, the endocrine glands, the emotional state of the subject and the calcium-potassium ratio in the skin. The irritability of the skin is apparently determined by the calcium-potassium ratio in the skin, which in turn is interrelated with the sympathetic nervous system, the endocrine glands and the emotional state.

The peculiar lability of the vasomotor apparatus in psychoneurotic patients, as manifest in disorders of the peripheral circulation, is important in a consideration of the psychogenic factors in diseases of the skin. The spontaneous occurrence of ecchymosis is not uncommon in hysterical persons.

In the following diseases of the skin, psychologic phenomena either play a motivating rôle or are a notable determining factor:

Blushing
Pallor
Cutis anserina } motivated by the emotions
Horripilation
Changes in secretion of sweat

(Dermatographia) → angioneurosis → erythematous eczema → angioneurotic edema → acute eczema (acute dermatitis)

Urticaria, acute or chronic

Edema (angioneurotic edema, edema in hysterics)

Pruritus, localized or generalized

Phobias referable to the skin

Neurotic excoriations: dermatothlasia (Fournier), self-produced lesions (no deception intended; variable psychogenesis)

Dermatitis factitia (mythomania of Dupré—self-produced lesions for deception

Fixed pain and sensory disturbances (topalgias of Blocq, for example, "burning tongue")

Angiospasm (so-called "dead" fingers)

Sudden loss of hair (alopecia areata) or a sudden turning to white (canities)

Trichotillomania

Trichokryptomania

Stigmas of the crucifixion

Tattoo

Psychogenically produced manifestations in the allergic state

Hysterical gangrene, bullous lesions (so-called pemphigus hystericus) and dermatitis dysmenorrhoeica are not included since there is much evidence that these disorders are self-produced. I do not share the opinion of some writers that herpes zoster and psoriasis have a psychogenic basis, but I agree that there is a psychogenic factor in the pathogenesis of dermatitis herpetiformis, of lichen planus and of the localized form of neurodermatitis.

Erythema of psychogenic origin, which commonly involves the face, may spread and involve the greater part of the cutaneous surface, virtually becoming erythematous eczema. In this event, it is usually blotchy and has sharply marginated borders. Dermatographia is a common circulatory disturbance of psychoneurotic patients. Localized edema and urticaria, as is well known, may appear suddenly after a psychic disturbance. A close relationship exists among dermatographia, angioneurotic edema, urticaria and dermatitis or acute eczema. These cutaneous reactions manifest additional steps in the same mechanism, which involves an unstable action of the sympathetic nerves, a vasomotor instability and an increased permeability of the cutaneous vessels of the neurotic patient. These cutaneous disorders which appear suddenly after a psychic disturbance, especially in psychoneurotic patients, may be justly designated as psychogenic.

Pruritus may appear at the site of the psychic fixation, the location of the itching frequently manifesting the influence of events, recollections or conceptions.

Suggestion and autosuggestion may play a part in the causation of itching. The desire to scratch is contagious, and psychic expression alone may suffice to initiate the sensation of itching. The sexual and lustful element in itching has been overemphasized. A considerable percentage of all patients with pruritus, especially those with pruritus vulvae and pruritus ani, are psychoneurotic and other symptoms of psychoneurosis are present.

Neurotic excoriations have a variable psychogenesis. This disorder may be an expression of a phobia (usually the fear of parasites), an expression of a tic or a phenomenon of displacement. Other instances may be classified as topalgia of Blocq or as Janet's obsession of shame of the body. In pronounced cases of neurotic excoriations, the psychogenesis is not easily determined and the cure is not easily effected.

The psychogenesis of dermatitis factitia concerns the rôle that suggestion plays in the causation of the self-produced lesions. Menninger claims that dermatitis factitia represents a localized self-destruction which serves simultaneously as an externally directed aggression of deceit, robbery and false appeal.

If one accepts the validity of reported instances of a variety of cutaneous lesions produced by suggestion in hypnosis, one can envision the stigmas of the crucifixion as cutaneous phenomena which are not beyond the realm of pathologic possibility. The tremendous nature of the mental stimulus which precedes the appearance of these stigmas and the emotional background of the subjects on whom they appear are of importance in the psychogenesis. The limitations of the influence of the mind over the body are still unknown.

In a study of the diseases of the skin in which psychic influences may play a rôle, the history is important in furnishing a clue as to psychogenic etiology. The type of patient and his emotional make-up are of importance in evaluating psychic influences. Attention should be focused on the circumstances associated with the onset and with the continuation of the pathologic condition, its occurrence after a certain act and its specificity referable to the time and place of its occurrence. Cutaneous phenomena characterized by vascular dilatation (erythema and exudation) which appear and disappear suddenly are suggestive of a psychic or an allergic causation.

PSYCHOPHYSIOLOGY OF THE SKIN. Presented by DR. PAUL SCHILDER.

Neither tactile nor optic sensations give one a definite impression concerning the skin. Knowledge of it is acquired by a continued dynamic process. Since the real and the imagined worlds are fundamentally the same, mental processes and emotions lead to sensations in the skin which are equivalent to perceptions. Furthermore, these sensations are connected with actual changes in the physiology of the skin. Emotional processes may lead also to organic changes in the skin. The basis for the conversion of symptoms to the skin is often some past organic disease, especially a disease of childhood. The diseases of the skin of one person may facilitate the production of symptoms of conversion in another person with whom he is in libidinous contact. Finally, the entire life history, both past and present, is of importance.

One case of psychogenic itching may be based on previous itching due to pubic lice, while another case of psychogenic anal itching may be associated with a secretion. Fear of castration, anal libido and organic changes experienced in early childhood also may be responsible.

Imagination may provoke sensations in the skin which have a definite meaning. The conscious wish may become sufficient, but generally the unconscious wish has the greater power. Spontaneous hemorrhages, blisters on the skin or urticaria may be the result of such unconscious attitudes. The changes in the skin are never isolated, but are merely the foreground of a total experience, the background of which is formed by the organic and psychologic past of the organism. The expression of the general psychosomatic change caused by emotions is dependent on the psychic attitude toward the different parts of the body in general, and especially toward the skin. The final formation of the psychosomatic change

depends also on the outward world. Infectious herpes labialis can be provoked by hypnosis. It is probable that various psychogenic dermatologic manifestations are due to specific conflicts in early life. There exists a differential psychology of the various psychogenic conditions of the skin. Anal itching has a close relationship to sadomasochistic tendencies. Psychogenic blushing is in close relationship to narcissistic attitudes and to the leveling of love to include others. Blisters and hemorrhages on the skin are closely related to a hysteriform attitude with a strong infantile Oedipus conflict. Changes in the skin that are due to organic diseases provoke a definite set of psychologic attitudes. Only by a complicated psychic process which goes through various psychologic layers does the patient become aware of these organic changes. The self-perception of an organic lesion of the skin goes through various symbolic stages by which it is brought into connection with the total experiences of the subject. Self-perception of the skin is a highly symbolic act.

A psychogenic manifestation in the skin always has a meaning; it may be conscious or it may lie in the sphere of symbolism or of instinct. There is no fundamental difference between imagined changes, so-called psychogenic manifestations, and organic lesions of the skin. They are all centrifugal, emanating from central conflicts of the personality to the periphery. Emotions and imaginations are never merely psychic, for the psyche is an organic agent. Neither does an organic disease of the skin remain at the periphery; it goes to the very center of the personality. Processes that are purely organic do not exist, for the organism is fundamentally a psychophysical entity.

DISCUSSION

DR. ABRAHAM WALZER: Dr. Klauder was probably the first dermatologist in this country, or at least one of the first, to publish original observations on the part played by the vegetative nervous system as the mechanism, and the calcium-potassium ratio of the skin and the blood as chemical factors, in the production of certain types of diseases of the skin.

With a subject of such vast magnitude and with time so limited, it may be advisable for me to discuss a type of the diseases mentioned tonight and analyze the symptoms in the direction of the possible mechanism of their production. How are the symptoms produced, and what is the relation to the psychogenic factors with which they are supposed to be connected? One of the best examples of these diseases is chronic or recurring urticaria. Whether the urticaria is toxic, allergic, psychogenic or otherwise, the symptoms are alike. Stokes has aptly labeled the wheals "cutaneous tears," but shed by the physician as well as by the patient, because there is no condition that so taxes the mind and ingenuity of the physician as do these chronic or recurring urticarias.

Now, how are the wheals produced? Experimentally one is able to produce wheals by a number of different methods and to study their various phases. Wheals can be produced by the intradermal injection of certain drugs, such as codeine and morphine, by cold, by heat, by traumatism in a susceptible person and by the intradermal injection of serum from an allergic subject into the skin of a normal subject, followed by the injection of the corresponding antigen at the same site. Wheals can also be produced experimentally through the gastro-intestinal tract by the injection of the serum of certain food-allergic persons into the skin of another. Then, when this person is fed the specific offending food the wheal will develop at the site of injection. While these variously produced wheals are indistinguishable clinically and histologically, each wheal undoubtedly went through a different mechanism in its formation. But they all had one important factor in common; namely, they all induced the liberation of histamine or a histamine-like substance as the end-result of their mechanism, and this substance, acting *directly* on the capillary vessels caused an increased permeability with the production of the resulting wheals. They are therefore independent of any nervous influence for their formation. Furthermore, the production of a wheal is not a simple angioneurosis, nor is it a simple angiospasm with a simple stretching of the capillary walls and oozing of the serum. It is a chemical reaction which induces the liberation of histamine or a histamine-like substance.

As to the mechanism of the wheal in so-called psychogenic urticaria, certain writers have suggested that in such urticaria the wheals are the result of one of two mechanisms: (1) The vegetative impulse attacks the digestive organs, with consequent digestive changes which influence the blood and then the skin—hence the wheal; (2) the vegetative impulse attacks the skin directly, with liberation of histamine or a histamine-like substance. Both of these conjectures appear to be purely hypothetical, and more than theory is needed for a final proof. It has never been established that histamine or a like substance is liberated as a result of nervous stimulation. While it is known that certain chemical changes take place in a nerve as a result of an impulse, no one has satisfactorily shown that a nerve so stimulated liberates histamine or a histamine-like substance at any of its points of contact. Therefore great care must be taken before it is assumed that, because a wheal is present which is unexplainable by any other means, histamine or a histamine-like substance necessary for its formation was liberated by psychogenic stimulation alone. Another factor, probably just as important or more so, is necessary in such cases in addition to the neurogenic stimulus before histamine is liberated, that factor is a certain type of skin. In other words, the psychogenic factor merely acts as a precipitating cause in a specially prepared site: an atopic shock organ—the skin. I shall refer to this again shortly.

One of the proofs advanced as to the causation of psychogenic wheals has been the results of therapy; i. e., the psychogenic causation of these wheals has been proved by their successful psychogenic treatment. The fact that a patient responds to psychotherapy is not an altogether satisfactory or sufficient proof that a condition of psychogenic causation has been treated. Credit for a satisfactory therapeutic result must be given to such factors as the patient's natural capacity for recovery, local therapy, rest, changes in climate, etc., and also to the fact that such good results are not often reported in many similar cases.

Dr. Schilder has touched on and elaborated beautifully the question of the multiplicity of causes of disease. I should like to emphasize that in a little different way. In attempting to treat disease, the physician often begins with a preconceived idea of one cause. In a search for the etiology, having found one cause that may or may not be important, he thinks that he is through and attributes all of the symptoms to it. In other words, every effect or disease has its single cause. It is now more or less agreed that disease is essentially the interaction of a soil (a complex human organism) and the seed (the offending factor). In both of these (the soil and the seed) reactions and changes are constantly taking place, and as a result of this union, each of these changes may produce its own symptoms. The effect of such a mechanism, that is, the interaction of the soil with its changes and the seed with its changes, is what is recognized as the symptom complex of the disease. What seems to be a single cause of a multiplicity of symptoms is in reality a multiplicity of causes producing the various symptoms. So with the psychogenic urticarias; while the psychogenic factors are unquestionably important, they are not the whole cause of the effect, not the whole seed, but only one link in the etiologic chain.

Summarizing the whole problem of urticaria, the probable mechanism of this type of disease is as follows: Many of the so-called psychogenic urticarias are in reality nonspecific reactions to a psychogenic stimulus in an atopic subject. Many of the patients are atopic. They give personal or family histories of such atopic diseases as asthma, urticaria, hay fever, etc. They have inherited an organ (the skin) which is sensitive to shock and as a result of a psychogenic stimulus the skin responds with urticaria. They may have other shock organs, such as the mucous membranes of the bronchi and nose, and as a result of similar stimuli may have symptoms referable to those, such as asthma. Experimentally one is able to produce such a phenomenon. For example, if the serum of a person who is sensitive to egg is injected into the skin of a normal subject and the next day the subject is fed an egg, a wheal will appear within a few minutes at the injected site. In half an hour or so the wheal will be gone. If the site of the injection is traumatized the next morning the wheal frequently recurs at the site of the previous wheal.

That is not a dermatographic wheal because wheals cannot be produced at any other site in that person; nor is it strictly speaking an egg wheal because it was not produced by the ingestion of egg. In other words, this specific site on the skin, or the shock organ, is in a receptive mood and, following various types of stimulation, a wheal may be produced. It is not a specific wheal because it was not reproduced by the original cause but by a nonspecific cause, such as trauma. This can be compared to the case of a hypersensitive person who has asthma due to ragweed which occurs during a certain part of the summer. If he catches a cold during the winter it may be followed by an attack of asthma. Or that same person during the winter, after a severe mental or physical shock, may have an attack of asthma. It is not a cold or neurogenic asthma; it is simply a nonspecific reaction in an organ (the bronchial mucous membrane) which is in a receptive mood and waiting to be teased along to produce a reaction.

I believe that the so-called psychogenic urticarias are not psychogenic in the true sense, but nonspecific reactions induced by nonspecific factors in an atopic subject. For this reason, treatment of the precipitating factor often clears up the attack.

In conclusion I wish to emphasize one fact. In searching for the etiology in these types of diseases, one should include all of the neurologic findings but be cautious in concluding that the cutaneous disease is necessarily neurogenic. On the other hand, the treatment of the neurogenic or other precipitating factors may be important and may be of aid in clearing up the attack. In other words, the usefulness of certain therapeutic measures may be more important than the truthfulness of a certain theory of the causation.

DR. E. D. FRIEDMAN: Since all modern thinking is colored somewhat by the new psychologic approach to man, it is perhaps logical that dermatology should also have come under the spell of the psychologic point of view.

I think that I must disagree definitely with Dr. Klauder, if I understand him correctly, in his attempt to make herpes zoster a psychogenic disease. It is known that a definite pathologic process underlies this disease, namely, an infectious ganglionitis. It is as logical to say that herpes zoster is a psychologic disease as to say that because simple herpes sometimes appears following injections of typhoid vaccine or after radiothermy, these agents caused the herpes. Both of these procedures simply activate the virus which is the ultimate cause of the herpes.

I should also like to hear some reasons for designating many cases of itching as of psychogenic origin. I assume that organic factors have been excluded. Perhaps Dr. Klauder in the detailed presentation of his cases has already produced the facts. I should like to know, for example, whether a careful study of the blood sugar and the basal metabolic rate was made and whether studies were carried out to exclude latent diabetes, hyperthyroidism or leukemia. In the case of the so-called hysterical ecchymoses, one would have to exclude thrombocytopenic purpura.

It is agreed that the involuntary nervous system plays an important rôle in many clinical entities. Vagotonia and sympathicotonia certainly are clinical concepts, but one must hesitate to ascribe to them direct and exclusive etiologic significance.

During the war the condition known as "main gelée" appeared as a result of injuries and was called "hysterical hand." Later it was found, however, that many of the cases were the result of injuries of the median nerve with typical causalgia, as described by Weir Mitchell years ago. The malady was an organic neurologic entity and not a psychogenic syndrome. Jackson in his textbook of dermatology, which was used in my student days, said in the chapter on warts; "It is strange that they often disappear and no one has seen them fall." I have been told that some dermatologists have postulated cures of warts with psychoanalytic methods. In such cases I should say that the cure was a *post hoc* and not a *propter hoc* phenomenon. And so I should state that while psychogenic factors exist in all forms of human illness, I for one am not willing to accept the dictum that they can serve as sole etiologic factors in diseases accompanied by the type of organic manifestations discussed this evening.

I am certain that one must agree with Dr. Schilder in his emphasis on the approach to illness through a study of the total personality. There is no question but that the study of man is necessary in every field of medical science. It is necessary in neurology, in dermatology and in internal medicine. The background (milieu) in which the person grows up certainly colors the later results of the conflict involved in dealing with the problems of life and with the difficulties into which the organism gets as a result of exposure to infections. I was greatly interested, as I always am, to hear Dr. Schilder explain his approach to medicine, because he started out as an organicist. I think that is after all the safest approach to the whole problem of clinical medicine.

DR. FOSTER KENNEDY: If one were to speak of and stand by only those things which one knows, there would be a great silence in the world. I do not think there is any doubt but that these deliberations regarding the psychologic origin of dermatologic ailments probably fill the hiatus created by the present ignorance of the pathology both of the skin and of the mind. Such deliberations keep the mind active, even if they do not always cure the disease. The skin is one's universe in little. It is the extension of oneself. It is no accident that the myth of Marsyas being flayed was really his depersonalization for his behavior. That is an oblation to the psychoanalytic school.

It is known that emotional conditions produce alterations in the skin. It is no accident that the skin and the brain are developed from the same layer in the embryo. There is a relationship, I believe, as well as an interaction between these two viscera. In hyperthyroidism, blotches come and go, playing like shadows over water on the skin of the patient. The skin is sensitized by the endocrinologic situation and possibly by the emotional situation thus engendered. I believe that stigmas of the crucifixion appeared in the saints, but I do not believe that the stigmas appeared entirely spontaneously. I believe that they occurred in persons with sensitive skins, with dermatographia (if one wishes to use the jargon of the day), and that the attrition of the nails on the palms produced the stigmas which would not have been produced in a person who was not sensitized endocrinologically and emotionally. The suggestion that herpes zoster is a disease of the mind and of the emotions rather reminds me of gathering simples in a field by the light of the full moon.

DR. JOSEPH HARKAVY: As an internist interested in allergy, I should like to try to coordinate the divergent opinions and see where they meet. I feel that each of the speakers has contributed to the understanding of the subject under discussion, namely, dermatologic lesions as influenced by the psyche, and every one is correct up to a certain point. What was most interesting to me was expressed by Dr. Schilder: that there are a dozen or more components in the production of any one symptom complex. These may be psychic to a certain extent; they may be organic, but finally, or rather, fundamentally, I think that they are allergic.

If by allergy is meant an altered capacity of the cell to react, it must be borne in mind that altered reactivity may be inherited or acquired and can be induced by many agents. In allergic reactions in organs of the body other than the skin, the same holds true. Such allergic manifestations, originally induced by a specific agent, as described by Dr. Walzer, recur on repeated stimulation by the same agent in the same tissue. The allergist calls such a reacting organ the "specific shock tissue." For instance, urticaria develops after a person has eaten shellfish. Repeated irritation of the skin by the ingestion of shellfish ultimately lowers the threshold of functional activity to such an extent that almost any stimulus may elicit a similar reaction, whether it is a psychogenic influence, food or the physical factor of cold or heat. The last two factors, by the way, are extremely important and I think have been neglected by most of the speakers.

When one talks about certain exciting factors as being responsible for a group of symptoms in the skin, the blood vessels or elsewhere, one has comparatively little knowledge of the physicochemical changes resulting in the human organism from such stimulation.

Lewis and Duke have shown that physical agents, such as cold, heat, stroking or insertion of a needle intracutaneously, may produce urticarial whealing, even as do eggs, fish or the stroking of a dog or horse in allergic subjects. Such wheals, according to Lewis, are associated with the liberation in the skin of a histamine-like substance. I have seen patients who are so sensitive to cold that immersion of the arm in cold water or the application of ice to the skin is followed by urticaria or asthma. Exposure to the sun may produce marked urticaria and dermatitis in certain persons who are susceptible to the actinic rays. Such results may also result from heat alone, no matter what its source.

There is therefore no reason why emotional stress accompanied by a rise of temperature cannot precipitate similar chemical changes, especially in fundamentally allergic persons, followed by manifestations comparable in every way with those originally induced by a specific excitant.

What effect the psyche can and does have upon the metabolic and physicochemical changes in the organism is still an unexplored field. Extensive investigation is yet to be done in order to determine the influence of psychogenic stimulation on the endocrine glands and on the autonomic nervous system, which may lead to changes in capillary permeability and to the liberation of hormones and a histamine-like substance, resulting in injury to the tissue.

I was, therefore, greatly pleased to hear what Dr. Schilder said this evening and to realize that at last the psychoanalysts are beginning to think and talk of a unified personality, influenced not merely by the psychologic but by the organic processes.

DR. BELA MITTELMANN: I should like to make a few remarks in connection with Dr. Schilder's and Dr. Walzer's statements as to the presence of both organic and psychic factors in some diseases of the skin. The organic factor is at times easily overlooked because of the fact that itching may be the only symptom of an allergic condition. The patient may not present any eruption on the skin and may have only the sensation of itching. This, as well as other symptoms, is often disregarded and considered psychogenic. I have one case in mind which I studied carefully, that of a patient who suffered from so-called neurotic excoriations for about ten years. This condition was so severe that the patient produced huge wounds on her face and actually destroyed the tip of her nose. In fact, she underwent three plastic operations to restore the shape of the nose and then started to carve the new flap. This patient, as I proved, had a definitely allergic background. She had itching of the skin and also vasomotor rhinitis. Earlier in life she had had urticaria. She was definitely sensitive to bacon and to any kind of pork but did not know it. If bacon was used in preparing her food, no matter what the food was, vasomotor rhinitis and itching would develop. Following the elimination of the allergic agents and with psychotherapy a cure was effected. Elimination of the allergic factors alone did not suffice, for without the neurotic element the patient would not have produced the neurotic excoriations. Besides, it was definitely shown that the itching and some other less definable sensations in the skin had not only an allergic but a psychic background. That is one type of case in which one can prove the presence of both factors.

PSYCHOLOGIC MOTIVES IN TATTOOING. Presented by DR. WALTER BROMBERG.

The material on which this brief study is based is taken from the Psychiatric Clinic of the Court of General Sessions. During the past year (1933) I had an opportunity in the routine examination of prisoners to study young men who were tattooed. Many of the principles brought forth tonight in the discussion of the psychology of the skin are illustrated by tattooed persons. The first striking observation which was made was that in all of the persons who were tattooed the decision to have a design applied was made impulsively. It was as if some great resistance had to be overcome. This resistance took two forms; in one, it was the overcoming of the social taboo against marring the skin; in the second instance it was the natural dislike to injure the narcissistic organ, i. e., the skin. From a

deeper point of view the skin is to most persons a perfect organ. It is sacred when it is unadorned (except by nature) and contains all of the elements of beauty. The skin is indeed a reservoir of narcissism. The impulsive decision to be tattooed was usually carried out under the influence of friends. Often men who were tattooed had the tattooing done while they were in an alcoholic state, and almost always the friends who accompanied them were themselves tattooed. Thus one sees in operation the influence of a latent homosexual factor. Another instance of the activity of the homosexual factor is expressed in the very symbolism of the tattooing needle and the fluid, the infliction of pain by an older man (i. e., the tattooer), by the absorption of sadomasochistic feelings in the subject and by the fact that the repression against homosexuality is weakened by alcoholic intoxication. A good case to illustrate this fact is that of a man who said that he was tattooed in Shanghai while in the navy during a drinking spree. Later, when he recovered from the intoxication, he was extremely sorry that he had had it done. The next time that he was in Shanghai with the same companion he had another tattoo "piece" put on, again under the influence of alcoholic intoxication. Later he was again sorry.

In a general way there are two types of men who bear tattooed designs. There is the older, usually more virile type of man, often a sailor, who is satisfied with his designs and who adds to his collection slowly over a period of years. This type is clearly exhibitionistic. At the extreme end of this group are the professional tattooer and the performer in a circus. The other group is comprised of young men who wish to bolster their feelings of inferiority by being identified with strong men, for instance, young sailors. These men quickly become disgusted with their pictures and do not have new designs put on except during a few years in their adolescence. The social taboo is on the surface in these men, and they will often say that the tattooing makes one look "vulgar and rough." Fundamentally, however, this feeling is a counterpart of the fear of castration. These men are apt to choose designs which express anthropomorphism, such as pictures of stalwart warriors, boxers, Indian braves and so forth. They feel the need of increasing their aggressive tendencies by wearing tattooed designs depicting strength. Exhibitionism and aggression are united, for example, in the sailor who is not afraid to display his tattooed designs or his bulging arm muscles, broad chest, etc. In this connection, it is interesting to see the relation of the tattooing of the sailor to narcissism. In the days of sailing vessels, sailors on their long trips frequently tattooed each other; in fact, that is thought by some to be the origin and development of American tattooing. In the older days sailors, because of their infrequent association with women, the absence of a heterosexual love object and their intimate association with each other, were apt to express their latent homosexual feelings in tattooing; moreover, the arms and the chest were frequently used as sites for their designs. According to the theory of "genitalization of the body" described by Lewin and others, in which the arms and even the chest are a phallic representation, tattooing on the body should provide a direct type of narcissistic and auto-erotic gratification.

It is difficult to study women in the clinic from the standpoint of tattooing because the material is poor, except for a few prostitutes who have obscene tattoo marks on the body. In this connection, it is interesting to note that about 1897 there was a wave of tattooing among women in this country, and the story is that one of the Vanderbilts started it with a tattooed butterfly on her shoulder. In that case the lifting of the social taboo was an important point. Apparently women can express more narcissistic erotism by clothes than they can by tattooing.

The types of pictures which are tattooed are strikingly diverse, but they are all illustrative of important principles. The most frequent type is the pictures of sexual objects, usually nude women accompanied by obscene statements. Frequently one sees homosexual pictures such as the design on a man's back of a cat chasing a mouse down toward the anus, in which the mouse has half buried itself. In the majority of instances the pictures of sexual objects proclaim the heterosexuality of man. At the same time they represent the final expression of the Oedipus situation combined with a marked sense of the guilt arising therefrom. This is nicely illustrated in the case of R. B., a young man of 21, who had on the right

thigh, a picture of a nude girl with the words "get hot" and on the right arm a picture of a girl's face. He said that he had felt proud of the pictures for about a month and then had became disgusted. On the left arm he had pictures of a cross and the word "mother" beneath it. He said that he wanted to keep all that "stuff" (girl's figure and head) on the same side of the body, because his mother's picture was on the left. His discomfort at having the tattooed designs was an expression of his feeling of guilt against an incestuous wish—expressed on the right side through the heterosexual designs and atoned for on the left side by the cross with his mother's name. The left side of the body is well known psychoanalytically as the side of guilt.

Another type of picture is the representation of ships, horses, historical figures, etc. These pictures show an anthropomorphic tendency and contain the elements of primitive art. They are also allied to the type of figure which seems to identify the person with certain times and events. Thus, some young men put dates, girls' initials and names of friends and sweethearts on their skin. I observed at Bellevue a boy of 16 with a depressive psychosis who said that his friends made a cross on the skin which they impregnated with dye so that they could tell a year later what had happened a year before! This is a curious example of the tendency to attain some sort of fixation in time and brings to mind the tendency of adolescent children to carve their initials and dates on trunks of trees and elsewhere. However, it is difficult to account psychologically for the presence of humorous tattooed designs, such as pictures of Mickey Mouse and characters from the comic strips.

A third and common type of tattoo design is the sadistic: pictures of skulls, daggers, blood, etc., all representing strong sadistic phantasies. I have often seen knives with an unusually liberal supply of blood. One of the tattooers of New York is famous for and proud of the livid dye he uses for representing blood. I have observed a defective boy, B. I., aged 18, who is extremely immature emotionally and physically as well as mentally. He bears the design of a large dagger cutting through a cuff of skin with a large amount of red blood dripping from the dagger and lining the pictorial cuff. In addition he has a heart tattooed in red, a cross with blood and several other religious motifs. This boy showed prepubertal sadism and aggression in his choice of designs. He is rather proud of the pictures, particularly of the dagger and the blood, and once remarked to me that the dagger was not really going through his skin! The expression in this case of the aggression which is part of the make-up of most boys in the prepubertal stage coincide with the boy's general immaturity.

A fourth type of frequent tattooing motifs is pictures concerned with death and questions of honor and guilt. Frequently these are represented by a picture of a cross with the word "Mother" beneath, with the date of her death or with no date if she is living. Often there is the picture of a skull with the words "Death before dishonor" above it. The religious motives are extremely common, pictures of the crucifixion, sometimes highly elaborate ones, covering the entire back. It is interesting that in the religious pictures the initials "I H S" (which translated, means Jesus, Savior of Humanity) are interpreted "I have suffered" or "I have sinned;" and "I N R I" (which, translated, means Jesus, Born King of the Jews) is interpreted "Iron Nails Rusted In." At the bottom of this type of picture, particularly tombstones with dates and names referring to the mother, is the strong feeling of guilt involving the Oedipus situation. It is interesting in this connection that rarely does one see designs dedicated to the father. A youth F. C., aged 19, with marked emotional and vasomotor instability and of an egocentric immature type, who has assumed an air of callousness as a shell to cover his feelings of inferiority, bears a design on his left arm of a skull with the words "Death before dishonor." He said he took the tattoo on a dare. From a psychologic point of view it was a challenge to his sadomasochistic and narcissistic tendencies. He threw further light on the situation by saying that he was a neat dresser and was particularly fond of form-fitting clothes but became embarrassed easily if people made remarks about his ultrastylish clothes. He said that his mother threatened to cut off his arm while he slept when he came home with a tattooed design.

Whereas he was previously proud of his design, he became extremely sorry that he had had it done and was frightened and ashamed. He said that he was ashamed because "people see you at the beaches and think you are a rowdy." This boy then transposed the fear of castration (in this case the threat was administered by the mother) to a fear of social condemnation, i. e., that people would not like him at the beaches.

The fifth type of pictures, in a rough way, represent those of the professional tattooer and the exhibitioner, who have new designs applied from time to time, some of the men being tattooed from head to foot. The pictures of the professional tattooers represent a special type. These men exhibitionize with little sense of guilt, regard their craft as a profession and derive constant gratification from the pictures on their skin. There are a few tattooers who are not tattooed extensively and are sorry that they ever went into the business. Most of the tattooers show by their placidity the lack of a feeling of guilt and the constant pleasure derived from erotization of the skin through tattooing. It is interesting to see that from the older men less material is obtained that helps in the psychologic study of tattooing. This is either because their sense of guilt has diminished as they grow older or because they belong to a group who are proud and derive pleasure from their designs. One case, that of J. B., illustrates this point to a certain degree. J. B. is a man of 40 who has been heavily tattooed from time to time. He has many designs on his arms and a large ship on his chest; the only comment he has made is that he did not mind the pain of any of them except the one on his chest. Another man who belongs in the same category shows some of the same features. G. R., aged 33, a ne'er-do-well, nomadic person, came from a good family. His father rose from the rank of a private to that of major in the army. The patient considered himself to be the "black sheep" of the family. He is a chronic alcoholic addict and obtained his tattoo designs while in the navy. He made a poor heterosexual adjustment in life and has had definite indications of a latent homosexual tendency. He once said that when "you are in the navy you feel bigger, like a real salt, when you are tattooed, but when you are out of the navy you feel sorry; it makes you look tough." In this case it seems clear that his attempt to identify himself with his virile and successful father, the professional soldier, was a factor in his getting tattooed. Here again the homosexual factors of a life in the navy and alcohol helped him to carry out the identification with his father through the tattooing. When he left that environment he felt ashamed of the pictures.

The development of tattooing in its psychologic implications can be understood by its close analogy to the psychology of clothes. As is well known, erotic gratification is derived from the skin and from the activity of muscles and joints predominantly in young children. With the approach of puberty the eroticism of the skin is displaced to the clothes. The pleasure that is derived from the skin is then transferred to clothes, where it remains, with individual variations, throughout life. This displacement is a normal reaction and accounts for the sudden attention to clothes which is exhibited by the average adolescent boy or girl. The high school sophomore, with his flashy ties, neatly pressed flannel trousers and colorful belt, illustrates this tendency. It is but a short step backward to transfer the eroticism in clothes to that of the body by means of tattooing. This regressive tendency quickly subsides in the average young person. This also explains why so many relatively normal young men are tattooed. In the professional exhibitor, however, who has a type of personality that is entirely different from that of the average person, the regression remains fixed and only gratification and pleasure are obtained from the tattoo pictures. The sense of guilt which immediately arises protects others from further tattooing; they merely have a fading picture to which they pay less attention later in life as a memento of this slight regression. The social taboo which operates in tattooing is seen to a lesser extent in clothes as the striking colors of the adolescent give way to the more conservative clothes of the mature person. This change occurs at the time when the libido is beginning to obtain sexual satisfaction along genital channels. At the same time, a movement is visible in the deeper psychologic layers of the psychosexual make-up which relates

to the Oedipus situation. On coming out of puberty the youth transfers his heterosexual love from his mother (Oedipus situation) to the outside world, i. e., to girls and women in his environment. In the process of transferring the Oedipus object to the outside world he usually makes his obeisance to the incestuous drive by the tattoo picture of a cross with the word "mother" under it or by others of that type. The case of R. B., already cited, illustrates this point.

F. M. is a youth of 19 whose great interest in aggressive sports masks a feeling of insecurity. He has marked vasomotor instability which is represented in frequent blushing and by his becoming easily embarrassed. The feeling of insecurity and the erythrophobia are probably guilty feelings related to masturbation. This boy is an enthusiastic member of an athletic club and is interested in boxing. He states that at the age of 18, when he had his first tattoo put on, he wanted to fly from the tattooer, but he had it done because of a feeling of bravado when among his friends. He said: "I was frightened about those needles; I got scared, but didn't want to be a coward. I wanted to run away as soon as I was finished. I had a feeling that was something like that when I first had intercourse. Some fellow wanted to break me in; I was very much ashamed and when I finished I couldn't stay there; I felt like running away." This boy has a tattoo picture of a boxer on his right arm and that of a girl on his left. Here we see the transfer of guilt from masturbation, similar to that existing at his first heterosexual relation, to the tattoo picture. C. O. illustrates a different source of the feeling of guilt. He is a man of 21 with a German father and a Puerto Rican mother. His father was a sailor and a captain of sailing vessels for thirty years; he was extensively tattooed over the arms, chest, back and body. The boy is proud of his father. He once said, "The sailors tattooed themselves in those days." In New York one time, while in the company of a German man who was tattooed all over his body, he allowed himself to have several pictures put on, but first he had his mother's name tattooed on his arm. He says that the tattoo did not hurt, but that he was a little frightened and, "I was kind of forced into it but I had my mother's name put on first." The boy says that his father was never sorry that he was tattooed but that he himself was a little sorry later, although on the whole he was rather pleased. Here we see obvious identification with the father. The actual seduction curiously enough was through a man who was equated to the father. At the same time he had his mother's name put on as a representation of the feeling of guilt involved because of the strong identification with his father, undoubtedly on a latent homosexual basis.

(The slides of tattoo designs which are demonstrated were taken from a book by Albert Parry [Tattoo, New York, Simon & Schuster, Inc., 1933]).

PHILADELPHIA PSYCHIATRIC SOCIETY

April 13, 1934

JOSEPH C. YASKIN, M.D., *President, in the Chair*

A CASE OF PSYCHOSIS DUE TO HYPOGLYCEMIA. DR. JAMES GREENWOOD.

For years, diabetes mellitus or hyperglycemia has been an important disease entity. What about hyperinsulinism or hypoglycemia? Are all disorders of insulin secretion of the deficiency type? There are about as many cases of hypothyroidism as of hyperthyroidism and a like balance between the opposite types of pituitary disease. Why, then, so many cases of diabetes and so few of hypoglycemia?

The syndrome of insulin shock is well known, but to diagnose hypoglycemia by this method would be equivalent to diagnosing a case of diabetes only if the patient were in a state of coma. Both insulin shock and diabetic coma are extreme conditions. Moderately severe diabetes, when untreated, may gradually undermine the

health of the patient. It seems logical to assume that hypoglycemia, if long continued, will do the same thing, but with different manifestations. Diabetes has its own group of symptoms; so also has hyperinsulinism. In the last few years much has been learned as to what these symptoms are. Many of them are mental.

Seale Harris, in 1924, in a memorable article on "Hyperinsulinism and Dysinsulinism," made the first contribution to establish the condition as a definite disease entity. This paper and most of those that followed reported convulsions or epileptiform attacks due to hypoglycemia. Allan, in 1929, reported two cases of hypoglycemia, in one of which there were temporary attacks of acute mania which passed off with the administration of dextrose. The other was diagnosed as hysteria until a blood sugar reading of 48 mg. per hundred cubic centimeters gave the clue to the diagnosis. Dextrose gave relief in this case also. Heyn, in 1932, reported a similar case.

By 1933, the following group of symptoms had been enumerated: nervous irritability and anxiety, weakness, fatigability, hunger, tremor, muscular twitching, lack of clearness of vision, diplopia, unsteadiness in gait, syncope, excessive perspiration, loss of emotional control, convulsions, coma and even death. Many of these symptoms belong to the so-called neurotic group, and to them one cannot help but add an equally large number of definitely psychotic manifestations as recorded in the literature and observed in patients. In spite of the fact that many of the patients in the cases reported showed obvious and at times extreme mental symptoms, little emphasis has been attached to the possibility that hyperinsulinism or hypoglycemia may be a cause of mental disease. Five such cases have been encountered at the Philadelphia General Hospital in the psychopathic wards during the past eight months.

A. H., a Negress, aged 45, was admitted to the service of Dr. Gilpin on Oct. 28, 1933, with the history that she had had severe headaches, starting two months prior to admission, and had been acting queerly and seeing peculiar lights at night. There were said to have been some ideas of persecution. In addition, there had been an increase in appetite, polyuria and nocturia, with urination several times nightly. When admitted, the patient was somewhat stuporous, but her eyes were open and there was a slight smile on her face. There was perfect catatonia, the limbs remaining in whatever position they were placed for from three to five minutes. She did not speak but made occasional movements with the lips as if attempting it. She did not respond to commands and was not suggestible. The eyegrounds presented a slight degree of arteriosclerosis. General physical examination gave negative results except for a palpable though not definitely enlarged thyroid gland. The blood pressure was 150 systolic and 90 diastolic. Neurologic examination gave negative results except for transient Babinski and Hoffman signs on the right. The blood urea nitrogen was 22 mg. per hundred cubic centimeters; the blood sugar, 45 mg.

A diagnosis of hyperinsulinism was made, and a glass of orange juice was given by mouth. Within fifteen or twenty minutes the patient was able to talk, though she was still somewhat confused. On the following morning she seemed much better and was able to give a good account of herself; she remembered nothing about the events which preceded her admission to the hospital. Speech was coherent and normal in every respect. The mood was neither elevated nor depressed and was in keeping with the thought content. She said that for the past several months when she went to bed at night she would see many queer things, balls of fire, various colored flashes of light and often the faces of different people whom she knew. There was good insight, in that she knew these visions were not real, and she suggested that they might be due to her imagination or to some fault of her eyes. That night she again saw the balls of fire and flashes of color, and in addition she could see the face of the doctor who had examined her that day. She would close her eyes but could not shut out these visual hallucinations. During this attack there was again mild but definite catatonia. On the following morning it was planned to perform a dextrose tolerance test, but while waiting for the specimen to be taken during fasting there was a recurrence of the hallucinations, with the additional symptom of extreme hunger, so that the patient slipped into

the kitchen unobserved and stole sufficient food to relieve her discomfort and also the hallucinations. Later tests gave the following values: blood sugar during fasting, 40 mg. per hundred cubic centimeters; one hour later, 131 mg.; two hours later, 200 mg., and three hours later, 124 mg. This curve is of the type that occurs in cases of the syndrome designated as dysinsulinism. The basal metabolic rate was plus 10. A roentgenogram of the skull showed a normal picture. Subsequent estimations of blood sugar during fasting yielded values of 113, 60, 60, 70 and 40 mg. A diet high in calories and in fat but relatively low in dextrose was then prescribed, and a glass of orange juice was given between meals and before going to bed. This is a modification of the ketogenic diet. No further mental symptoms occurred during the remaining twenty days which the patient spent in the hospital. This case not only illustrates the rôle of hypoglycemia as a cause of mental symptoms but presents an unusual picture in the perfect catatonia and visual hallucinations.

There is little doubt that hyperinsulinism or hypoglycemia is a definite clinical entity. How frequently the cases occur will not be known until one has learned to watch more closely for them and to look for something in addition to the classic picture of insulin shock. One can no longer regard a blood sugar content as low as 60 or 65 mg. per hundred cubic centimeters as being without clinical significance. If estimated accurately, these findings have a definite meaning and should be investigated. It is well to remember that many of the manifestations are neurotic or psychotic.

DISCUSSION

DR. ALFRED GORDON: I can add two cases to those of Dr. Greenwood. One patient is being treated for sciatic neuritis and at the same time for diabetes. She has been given insulin. There was great tolerance in the beginning, but in the last few months neuropsychiatric symptoms have developed. After 10 units of insulin is given, the patient has tremors. I witnessed one attack. There were muscular contractures, and the patient was confused and said that she saw lights before her eyes. Having noticed this peculiarity I advised that each time insulin was given several lumps of sugar should be available; after taking 10 units of insulin she takes one lump and in a short time another; following this she lies down, and the symptoms disappear. Another woman, with manifestations of a disorder of the endocrine glands, had 145 mg. of sugar per hundred cubic centimeters in the blood and was advised to take insulin. Five or ten minutes after an injection she experiences vertigo followed by visual hallucinations; she is disoriented for a short while. This patient also takes lumps of sugar, and the symptoms disappear.

DR. MEYER K. AMDUR: Has Dr. Greenwood noted a relationship between dipsomania and hypoglycemia?

DR. JAMES GREENWOOD: Rather frequently diabetic patients exhibit (due to overdoses of insulin) symptoms similar to those of spontaneous hypoglycemia; it is owing to these observations that I have looked for this condition in cases in which insulin is not administered. I do not know about dipsomania. I have seen a markedly low sugar content in patients with alcoholism, but have not looked for this in cases of dipsomania. Some of the most marked cases, which had been considered instances of acute mania, were later found to be cases of alcoholism with low blood sugar. The pancreas is not the only organ involved in hypoglycemia. The liver certainly has a definite function in sugar metabolism. Perhaps in toxic states the liver is damaged, and for that reason glycogen is not produced and when called for is not there.

A CASE OF SCHIZOPHRENIA OCCURRING IN CHILDHOOD. DR. ROBERT S. BOOKHAMMER.

Psychiatrists have become interested in the psychoses of childhood in recent years. The literature on the subject, however, is meager when compared with the vast amount written about psychoses in adolescence and in adult life. Berkham,

in 1750, reported a case of melancholia in a child. In his "Treatise on Insanity," Esquirol recorded three cases of frank mental disease in children seen in his own practice and referred to a boy in London who had been maniac since the age of 2. In reviewing five thousand consecutive admissions to mental hospitals, Strecker found eighteen instances of psychoses in children, four of these being cases of dementia praecox. Rhein, in 1914, collected forty-four instances from the literature and added four from his own records. In a paper read before this society in 1924, Burr spoke of a boy, aged 12, whom he considered to be suffering from hebephrenic dementia praecox. A. A. Brill had two catatonic children under observation; both were girls, one aged 4½ and the other aged 6. Six cases of dementia praecox were reported in 1932 by Potter, who had studied them at the Psychiatric Institute in New York. Kasanin and Kaufman found twenty-one schizophrenic children in a group of six thousand patients admitted to hospitals.

Although mental disease occurs infrequently in children, it is likely that many cases are overlooked. Peculiar emotional reactions and behavior in a child are apt to be considered to be due to mental deficiency, encephalitis or delinquency. The traditional point of view concerning dementia praecox has led one to think of it as chiefly a disease of adolescence and of early adult life. Since first introduced as a separate disease entity by Kraepelin in 1898, its occurrence in this period of life has been stressed.

It is not uncommon for psychotic children to be sent to institutions for the mentally deficient. This has been noted recently by Greene, of the Walter E. Fernald State School, in a paper read before the American Association on Mental Deficiency. In his summary he stated that psychosis in children is not as infrequent as is generally believed and that there is special need for study of the symptoms, etiology and treatment of psychotic disorders of childhood.

The symptoms shown by children in psychotic reactions have been likened to those of primitive races. Quoting Kraepelin, Strecker stated that among the Javanese with dementia praecox there was preliminary excitement, passing rapidly into silly dementia. Catatonia was infrequent. Hallucinations were rare, and delusional formation was elementary. So, in the cases of children one finds blocking, condensation, perseveration, incoherence and mutism. There are emotional inadequacies and distortions of feeling, alterations of behavior with excitement or cessation of motility. Paranoid ideas and delusions are not often reported.

This boy, aged 13, is the son of Austrian Jewish parents; the father, who was a patient at the Philadelphia Hospital for Mental Diseases, the diagnosis in his case being dementia praecox, died at the hospital a week following the patient's admission on Oct. 5, 1933; the mother is poorly educated and unintelligent but is in fairly good health; one brother is apparently normal.

The patient was born and reared in Philadelphia. Birth and early development were normal. He walked at 1 year and talked at 18 months. He had the usual diseases of childhood, including scarlet fever. Mental symptoms became noticeable at the age of 7, when he was admitted to the Mount Sinai Hospital. At that time he was said to show disinterestedness and queer behavior; he refused to talk and laughed to himself. A diagnosis of mental deficiency was made. For reasons which are not clear the patient was referred to the outpatient department of dermatology and syphilology at the University of Pennsylvania Hospital. Several serologic tests were made, and because of two medium-positive reactions to Wassermann tests with the Kolmer antigen he was given arsphenamine for a year and a half. All Wassermann tests of the blood and spinal fluid made subsequently have been negative. He received another course of treatment in 1929. At this time he was 10 years old. The records of the department of dermatology show that some physicians thought that the diagnosis of congenital syphilis and later of juvenile dementia paralytica was an error. The father, mother and brother have never shown any clinical or serologic evidence of syphilis.

From September 1925 until the spring of 1933, the patient attended school for sixteen terms, reaching the fifth grade only. In 1928, a psychometric test gave an intelligence quotient of 102. Another test in January 1934 gave an intelligence quotient of 59, with a mental age of 8 years and 3 months. The comments of the

teachers throw more light on the condition than any information from the mother, who has not been able to give a satisfactory history. According to the teachers the patient was never quiet, was afraid of other boys and took things, not to steal but because he had no sense of property values. He was ill treated on the street. He went to school at times with his face scratched and gave weird explanations. The children thought that he was queer and he did not mingle with them. The boys thought that he was a "nut."

In August 1933, the patient's mental symptoms became intensified. He became fearful, screamed, refused to eat and could not sleep at night. He spoke of his father, now in the hospital, and begged his mother to keep him from going insane. He made many statements which the mother could not understand. She said that they had no meaning. Through a social organization, the aid of which the mother enlisted, arrangements were made to take the boy to the psychopathic ward of the Philadelphia General Hospital. On his way there he shouted to the driver, referring to other cars on the road: "Smash them, smash them, we must lead the way." In the psychopathic ward he was noisy, destructive and agitated. He stated that boys in his street "double-crossed" him. He said they called him "Tweedle." He remarked, "Oh that's rotten, you don't need to do that, it's a lot of hell." He admitted having hallucinations and said voices told him all kinds of rotten things. He saw people in his room and thought that the world had been turned around.

Appendical colic developed, and the appendix was removed. Following this the boy became resistive and negativistic; he was in this state when admitted to the Philadelphia Hospital for Mental Diseases. His attention could not be obtained. He held saliva in his mouth and had to be fed by spoon. He appeared to be actively hallucinating. During the month following admission he did not talk and seemed unaware of his surroundings. Gradually he emerged from this catatonic state, which was replaced by silliness and mischievousness. The condition has been stationary for the past two months. He no longer hallucinates. He has expressed no delusions. The chief symptoms are emotional inadequacy and an apparent mental deterioration. The physical condition, on repeated examination, has shown no gross organic changes, and all laboratory studies have given negative results.

WITCHCRAFT AND HUMAN CREDULITY. DR. THEODORE DILLER, Pittsburgh (by invitation).

Belief in witchcraft is the common heritage of mankind and belongs to no age, race or religion. While it has always existed, it was especially prevalent in the seventeenth century, when it was held by practically every one, learned, ignorant, Protestant and Catholic. There were many trials and executions, probably as many as 100,000 in the seventeenth century. While it appears that belief in witchcraft has faded from the earth, it is held still by a few persons here and there. Mankind is strangely credulous, and the trust which was placed in witchcraft in the seventeenth century is now given to somewhat different but essentially similar cults, such as spiritualism and Eddyism; indeed, even in orthodox medicine some superstitious qualities are attached to various procedures.

Today science is greatly exalted; some people give to it a somewhat superstitious faith such as obtained among religious people three hundred years ago. It is rather pitiable to contemplate the overestimation which many people give to the accomplishments of science, great and varied as they are. Here I may quote, as most appropriate, a paragraph from Professor Frazier's great work, "The Golden Bough":

"The circle of human knowledge, illuminated by the pale, cold light of reason, is so infinitesimally small, the dark regions of human ignorance which lie beyond that luminous ring so immeasurably vast, that imagination is feign to step up to the borderline and send the warm, richly colored beams of her fairy lantern streaming out into the darkness; and so, peering into the gloom, she is apt to mistake the shadowy reflections of her own figure for real beings moving in the abyss. In short, few men are sensible of the sharp line that divides the known from the unknown; to most men, it is a hazy borderline where perception and

conception melt, indissolubly into one. Hence, to the savage, the ghosts of dead animals and men, with which his imagination peoples the void, are hardly less real than the solid shapes which the living animals and men present to his senses; and his thoughts and activities are nearly as much absorbed by the one as by the other. Of him it may be said with perhaps even greater truth than his civilized brother, 'What shadows we are, and what shadows we pursue!'"

The physician, like his patient, has indulged in countless numbers of beliefs regarding the theory and cure of disease which he has afterward abandoned. There is no need to recite all this; but I must mention a discarded remedy of which I have personal knowledge—the Bergeon treatment for tuberculosis. This so-called "cure" came into vogue while I was a resident physician at the Philadelphia General Hospital. The remedy consisted in blowing hydrogen sulphide into the rectum on the assumption that it would be absorbed and would produce a noxious effect on the bacilli of tuberculosis. Soon after its introduction, large numbers of tuberculous patients in Blockley were being treated thus. Resident physicians went from bed to bed with a rubber gas bag and sat on it, thus forcing the gas into the rectum. Practically all patients improved, some of them rapidly and to a remarkable extent. There was enthusiasm on all hands, shared alike by physicians, patients and their friends. Nearly all the patients gained in weight, one of them 15 or 20 pounds (6.8 to 9.1 Kg.). This shows again that psychic influences may benefit not only the mental state but the physical well-being of a patient. This was one more case of the deceived deceiving, or the blind leading the blind. It affords an illustration of the vast and powerful effects of psychic influence when there is thorough and complete belief.

The physician is made of the same stuff as are other men. To be sure, his special training alters him, but it changes him little in regard to the great fundamentals of life. In other words, he is a man among other human beings with a little special knowledge and possessed of the same hopes and ambitions as other men. Therefore, possessed of an emotional and an intellectual nature, as he looks at the world he finds a struggle between these two. He sees material things; he knows in his breast that there are hope and fear and belief, and he sees these all about him. His job being the conservation of health and the prevention of disease, he must consider man in his entirety, his body and his mind. Physicians concerned with the most mechanical of things—surgery—must consider the mind; but all physicians who are not surgeons are especially concerned with it. Indeed, it may be said that all diseases are mental or have a mental aspect, even such grossly organic conditions as fractures or tumors. There is widespread belief that there is a remedy for every disease. This has led men to search all parts of the world for drugs and remedies, and following his usual bent the physician attaches to various remedies a significance which their material hardly permits. Montaigne well pointed out that the element of strangeness and rareness, the disgusting nature and the bitterness, is the quality that makes many remedies potent. Therefore, procedures which are novel or unusual have always had a vogue. Things which are mysterious, such as electricity, x-rays, massage and sunlight, always make an appeal. So it happens in medicine, as in other fields of life, that one finds oneself confused with things that one knows and things that one believes. It is the endeavor of the medical profession to add more and more that is known and to subtract more and more from what is believed. This has been done to a considerable extent, but it will never totally remove things believed.

Several years ago, Osler remarked that Mr. X went about the country getting nothing but treatment when what he needed was a diagnosis. Today this saying could be paraphrased: Mr. X went about the country getting nothing but diagnoses when what he needed was treatment. Today, with the elaborate machinery for diagnosis, including many complicated laboratory tests and the weighty expenses which accompany them, is it to be wondered at that cultists who make a brief examination and immediately, without waiting, offer a remedy make a strong appeal to the sick man? Would it not be well to learn a lesson from this, and if prolonged and detailed examinations are necessary would it not be wise and

sensible and humane for the physician to offer the patient some remedy immediately, even though it may be temporary or pearhaps wholly psychic?

Human beings are ever hopeful. Orthodox medicine has many failures and often it is slow. People are impatient and leave the established physicians to go to those who administer immediately to their wants or their needs, or who promise them what they desire—a cure. These they can always find and always have found. So it happens that orthodox medicine is shadowed and surrounded by a system of cults which promise that which orthodox medicine cannot and will not promise or offer. Hence, human nature being as it is, there is a steady and insistent demand, one may say, for irregular practices. In other words, orthodox medicine cannot now and never will in the future altogether satisfy the demand and hopes of those who are ill. Outside of orthodox medicine there will always be groups and systems which will promise what it cannot promise.

Ever since the regular medical profession grew into being, there have been quacks, humbugs, absurd systems and cults. Today witchcraft has almost disappeared, but the cults are here; some are dying out and some are coming on, strange, bizarre and novel. Each in its turn will make its appeal and will fit in with some of the various groups and temperaments. Wherever truth stands, error will be found close by. The church has struggled with heresies since her very beginning; and so with regular medicine. True, medicine has emerged from the past and erected a scientific foundation which makes it vastly superior to that of the middle ages, or even to that of fifty years ago, but it can never be, or hope to be, altogether exact. It must always deal with things intangible as well as with those that are subject to the senses. So long as this is true it will be subject to error, doubt and controversy; it will always fall short of doing completely that which it desires to do. It will suffer because of too little and of too much belief on the part of physicians and patients alike. The most one can hope to do is to delimit and segregate quacks, humbugs and the various cults. There is eternal warfare between orthodoxy and heterodoxy in medicine as well as in the church.

FOLK BELIEFS AS TO THE ORIGIN AND CURE OF DISEASE. REV. THOMAS R. BRENDLE (by invitation).

To understand folk ways of healing one must know the folk conceptions of the origin of the various ills of man. As long as common people retain the traditional concepts of the origin of disease, so long will they retain the traditional ways of healing. Three streams of medical belief and practices mingle in the lives of people: the ever-growing stream of scientific medicine, the ever-dying stream of household medicine—the householder being his own physician—and the ever-dying stream of occult and sympathy medicine.

To the folk mind an ailment has either a known explicable origin or an unknown inexplicable origin. When the origin is wrapped in obscurity, the ill may be ascribed to an occult agency, to a demon or to a witch. Here, then, relief is sought in occult practices. Nevertheless, with the advance of science, health instruction in the public schools and the activities of the state department of health, belief in witches and witchcraft would die a natural death if it were not for the charlatan "witch doctor." Belief in fortune telling would soon disappear if it were not for the professional fortune teller. Then, too, when medicine fails or errs the ordinary man is prone to turn to some faintly remembered traditional treatment.

At present, among the so-called Pennsylvania Germans, belief in witchcraft is almost extinct, despite the impression given by newspapers and by the books of reputable authors. Witchcraft has often been seen where there really is none. The decorative circles, "wheels" on the barns, which are so frequently pointed out as "witch signs" have nothing whatever to do with witchcraft. Nor must the application of sympathy medicine, erroneously called by the Indian name pow-wowing, be confused with witchcraft. Where a belief in witchcraft occurs, it is found in a certain stratum of intellectual development: "Given a family that lives in a narrow circle, that is more or less self-contained, whose relations with

the world round about are limited, that does not enjoy a goodly portion of the graces of the broader life—given an inexplicable ailment, and given the memory of a witch tradition, and you have the ground bed for a belief in witchcraft."

DISCUSSION

DR. E. D. BOND: Let me try to add to these two interesting presentations three short examples which will turn the matter of magic back to clinical psychiatry. First, I wish to call attention to what a boy, aged 8, who was at the Pennsylvania Hospital for bad behavior, remarked to a psychiatrist in an interview. He made sharp gutteral sounds and then told the doctor what magic he had done. He would say: "Grrr—See what I have done. Grrr—look at me, my ears are gone. Grrr—my hands are gone. Grrr—now they are on again."

On pages 334 and 335 of "Clinical Psychiatry" by Strecker and Ebaugh, there are some interesting pictures of magic attitudes.

A third example of interest is the case of a girl who at 4 or 5 was afraid in her play to wave her magic wand for fear she would turn her playmates into gold. That patient at the age of 24 has dementia praecox and has delusions which carry on the ideas of magic which she had as a girl of 4 or 5.

DR. C. W. BURR: I wish to refer to three books, all of considerable interest, and I confess that I doubt if the members have heard of one of them. The history of the "Restoration Extraordinary" was written in 1710 by a French abbé, and like many of them he was not a priest but a dramatist. His work was to entertain, and he allowed God and the curé to take care of souls. He did not believe in witches in any form. He thought that the greatest weapon would be, not a serious book, but a book which made fun of witches. He followed the example of Cervantes and, just as the latter used Don Quixote, he used a similar character to present his thoughts. The hero was supposed to believe that he was bewitched by a lady, and his adventures are reported in true French style. People, in speaking about the abbé's books, claimed that they were his only sins, to which he replied that the public paid penance by buying them.

The second book is Joseph Granville's rather famous book. Granville's ghost got money from me as a young man by having written "Skepsis Scientifica." I was a skeptical young man in the proper sense, and I supposed that this would be a book that would be meat to my soul; so I spent the money, but when I came to read the book I found that it was a defense of witchcraft. The book did not deal with "disbeliefs" but concerned belief in the things one should believe in. My edition is that of 1689. I forget the year of the first edition, but it was some twenty or thirty years before that. The book also had a tremendous effect among people believing in witchcraft.

One of the earliest antagonists in England was John Webster, a practitioner of physics. He was not willing to say there was no truth in witchcraft, but he did things by methods of indirection. He showed what symptoms the disease of melancholia would produce and how insanity could lead people to believe and say that they were witches when they were not. He also claimed that witchcraft was within the bounds of possibility, and he would pretend that he had counterpower.

John Scott was a mud slinger and a grafter. He would not find witches until he had 20 shillings, and even then he had to be paid for every witch he had punished or hanged. His death was mysterious. There were two stories concerning it. One was that he himself was accused of witchcraft and was burned as a witch or hanged, and the other that he disappeared and was not heard of again. He was as black a scoundrel as ever lived. He made money by perjury and by acting on the superstition of honest people. There is no evidence that he believed in witchcraft.

One of the most remarkable and earliest books against belief in witchcraft in England was that of Reginald Scott, which had a remarkable history. The first English edition appeared in 1574. There were a Dutch edition in 1609, and another in 1637, two English editions in 1651, and another in 1654. Another edition followed

in 1665, and then in 1886 there was a reprint of it, either in New York or in London. The copy I have is that of 1665. It was certainly one of the important books.

One of the things of great consequence arising from the witchcraft trials in New England was that a clergyman in Boston, who "smelled a rat" and thought that there was a good bit of humbug about witchcraft, accused the Mathers, father and son, of doing wrong and read a paper against belief in witchcraft. The paper was reprinted in London and had large sales; it was one of the things which opened the eyes of Parliament in London to the cruelty of the practices arising from belief in witchcraft and put a stop to them.

Dr. W. Cole Davis: These cases are not confined to Pennsylvania. I saw a patient in the Atlantic County Hospital for Mental Diseases this morning who had dementia praecox and had been sent from near Richland. She was the daughter of a farmer and had been tied to a chair and beaten repeatedly in an attempt to drive out the devils that possessed her.

Dr. Theodore Diller: Common delusions in dementia praecox, for instance, animal magnetism, appear to be to a considerable extent like many of the beliefs in witchcraft. Indeed, I have no doubt that many cases of witchcraft were cases of dementia praecox.

Book Reviews

Diseases of the Nervous System. By W. Russell Brain. Price, $8.75. Pp. 899. New York: Oxford University Press, 1933.

In a book of about 900 pages there is a discussion of the whole nervous system, including the neuroses. The book has an unusual feature in that there is a discussion of the nervous system in relation to life insurance. Necessarily, the discussions are short; while some subjects are adequately covered, many are not. The author first considers disorders of function in the light of anatomy and physiology. It is interesting in this connection that in the consideration of pyramidal syndromes he follows the outline of Hughlings Jackson in discussing positive and negative symptoms. This is an admirable attempt, but in the rest of the book it is not carried out. This is to be regretted, for it would have been a distinct gain to have such a division carried through a textbook of neurology. It is to be hoped that some author will do this.

As an example of the space given to the various topics, the whole subject of aphasia is covered in 9 pages, and apraxia and agnosia are covered in 2. The discussion of the fifth nerve, with its diseases and methods of treatment, including injection, takes up 13 pages. The account is brief but adequate. The same can be said regarding the eighth nerve. The recognition of glossopharyngeal neuralgia is attributed to Wilfred Harris, although some years before an American described it. The subject of intracranial tumors takes up about 50 pages. The classification of the types of lesion is that usually adopted. The discussions are cursory but cover the main points. There is a chapter on intoxications and deficiency disorders. Addiction to alcohol, morphine, heroin, cocaine and other drugs is taken up. It is interesting that in this group is included the discussion of polyneuritis. The subject of injuries to the brain takes 15 pages; this includes intracranial injuries at birth. Migraine is discussed among paroxysmal and convulsive disorders. The discussion of the neuroses, which takes up 24 pages, is hardly adequate, and it would have been much better to have left it out. Lastly, there is a useful list of references.

The day for textbooks of this sort has long since passed. It is practically impossible to cover the whole realm of neurology, including the psychoneuroses, in a book limited to 900 pages. There is not enough material for the student of medicine and certainly not enough for the student of neurology. On the other hand, the general practitioner might find the book useful.

Neurologische Begutachtung. By F. Stern. Price, 7.80 marks. Pp. 189. Berlin: Julius Springer, 1933.

In this book Stern gives a brief survey of the whole field of forensic neurologic examination and testimony. It is divided into a brief "general" and a longer "special" part. The former deals with the most important medicolegal problems, viz., invalidism, inability to work and consequences of accidents and injuries received during work, and with methods of examination and formulation in these different types of cases. In the special part the author discusses the neuroses and organic conditions. There is a brief index of subjects.

The necessity for such a book is not entirely evident. The student or physician who must give expert testimony in neurology will be better prepared if he studies one of the comprehensive textbooks of neurology. The primary requisite for an expert physician, even though he is "only the tool of an official agency," is the fullest possible knowledge of his specialty rather than any acquaintance with general formalistic principles. To give an example: On page 151 Stern states categorically: "The possibility that cerebral arteriosclerosis is provoked by trauma of the head I deny entirely," only to state a little later: "It must be admitted

that arteriosclerotic persons cannot endure cerebral traumas as well as those with healthy vessels." Between these two sentences lies the whole field of the concrete evaluation of the development of symptoms in neurology. In discussing lead poisoning, Stern states that he has never seen a case of lead intoxication after gunshot wounds in which the bullet remained in the body. Such cases have been described, however, in the literature. There is no discussion of alcoholism, and the word does not appear in the index.

The chapter on neuroses remains on formal ground. Neuroses and psychoneuroses are characterized as those "nervous disorders or subjective states of suffering which have occurred on the basis of an abnormal mental constitution or (as equivalent) of an abnormal irritability of the nervous system" (page 41). There are few literary references.

Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment. By W. E. Dandy. Cloth. Price, $5. Pp. 169, with 120 illustrations and bibliography. Springfield, Ill.: Charles C. Thomas, Publisher, 1933.

This valuable monograph is founded on a series of twenty-one cases observed by the author and in which he operated. The cases are described in sufficient detail, and the illustrations are plentiful and graphic. Five of the tumors were colloid cysts; the remainder were chiefly gliomas of various sorts. Dandy's operative results were remarkable. In all instances the tumor was removed. The gross mortality was 33.3 per cent; however, in the last fourteen cases there were only two deaths. Forty-seven cases are assembled from the literature, in none of which the diagnosis was made during life; this should not be interpreted, however, to mean that no successful operations have been reported.

From an analysis of the whole material, Dandy concludes that the symptomatology of tumors in the third ventricle is not particularly characteristic. Suggestive manifestations are: (1) loss of pupillary reflexes; (2) intermittent attacks of various kinds, e. g., headache, weakness, dizziness and loss of vision; (3) bilateral ophthalmoplegia, and (4) possibly loss of high tones in the audiometer curve. In three instances there were roentgenologic changes.

Ventriculograms were diagnostic aids in the seventeen cases in which they were used. If the foramina of Monro are plugged, air does not pass from one lateral ventricle to another (unless through a pathologic defect in the septum). If the third ventricle is partially filled by the tumor, it may be possible to recognize this fact.

The operative approach varied. For anterior tumors it was usually through the frontal lobe. For cysts of the septum it was through the body of the corpus callosum. Tumors of the pineal gland were attacked between the occipital lobes through the genu.

The pathologic aspect of the subject receives rather scant attention. The author states: "The subdivision of glial tumors upon finer cellular studies I believe to be most unfortunate and misleading." Photomicrographs of most of the tumors are given, however, and this is perhaps more important than a rigid nomenclature. The literary style could be improved by attention to tenses and pronouns. The book should, however, be in every neurologist's library.

Die parasagittalen Meningeome. By H. Olivecrona. Price, 24 marks. Pp. 143, with illustrations. Leipzig: Georg Thieme, 1934.

This monograph is based on the material of thirty-four cases observed by the author. It may be regarded as a continuation of the studies of Cushing and of Elsberg on the same subject and follows them almost point for point. A large number of excellent histories are given in detail and are well illustrated with photographs, graphic drawings, roentgenograms and diagrams. There were in this series an astonishing number of bilateral meningiomas—in all, thirteen—communicating with each other through the falx cerebri and sometimes through the sinus. In several instances the sinus was obliterated by the tumor. The character-

istic changes in the overlying bone and in the vessels are well described and illustrated.

The chapter on pathology is contributed by Henschen and contains some striking illustrations of villous projections of tumor through the dura. The description of the symptomatology and of operative technic appears sound, but is not particularly new. In the author's experience, ligation and resection of the longitudinal sinus appear to be safe when the sinus has become obliterated by a tumor, but not otherwise. Arteriography by means of thorium dioxide solution was carried out in several cases without ill effects and appeared to be of great value in diagnosis.

The literature is well covered, and the volume should be of interest to all neurologists.

Die psychopathischen Persönlichkeiten. By Kurt Schneider. Third revised edition. Price, 5 marks. Pp. 123. Vienna: Franz Deuticke, 1934.

This is the third edition of Kurt Schneider's familiar book on psychopathic personalities, the first edition of which appeared more than ten years ago. In its first edition the book was a welcome survey of a chapter that had always been a stepchild of clinical psychiatry. The present edition contains a number of additions and changes, but the main substance of the book is the same and so needs only brief comment.

The fact that the author has brought the book up to date (from his point of view) reveals certain of its defects more clearly than was apparent in earlier editions. On its first appearance, the book was considered a conservative presentation of the subject. In the intervening decade so much progress has been made in dynamic psychology, and psychopathology that the present up-to-date edition strikes one as not merely conservative but definitely backward. It is no longer possible to neglect so completely all the data unearthed in this field by psychoanalytic and dynamogenetic investigations. In fact, the extent to which the clinical formulation can be harmonized with the more clearly defined and well established mental mechanisms is today the chief problem in any discussion of psychopathic personalities. As a motto for his book, Schneider takes a sentence from Koch's book on psychopathic inferiority published in 1888: "One gains there some undreamed-of views into the life of human beings and into the motives that operate in them." In 1934, a much deeper psychologic penetration of the subject and a much wider sociologic outlook than this book offers are necessary to justify placing such a sentence as the motto of a work on psychopathic personality.

Mental Healers. By Stefan Zweig. Price, $3.50. Pp. 363. New York: Viking Press, Inc., 1932.

It is not often that a layman can appreciate the intricate problems involved in psychotherapy and the quest which the best medical minds have made for centuries to understand what takes place in a therapeutic relationship. It still is not known why patients get better and how diverse technics produce exactly the same results.

Zweig discusses the biographies of Mesmer, Eddy and Freud. The first is by far the most interesting and the most penetrating and gives probably the best insight into the subject's genius. There is a complete identification of the author with Mesmer, and one can always see how Mesmer tried various methods to learn in what way his patients could be benefited best. One also sees a keen, intelligent, scientific mind, with humility and criticism, so that one gets an altogether different picture of Mesmer from the usual idea of a mixture of a great personality and a charlatan. The biography of Eddy is interesting in the sense that the author stresses how her work did not really begin until she was quite old and how her power grew in spite of constant physical infirmities. The account of Freud is perhaps the weakest of all. One gets the impression that the author knew him personally; the biography is a neighborly account rather than a penetrating analysis of a genius.

The book is worth reading.

Adolescence: Life's Spring Cleaning Time. By Beverley R. Tucker, M.D. Price, $1.25. Pp. 121. Boston: Stratford Company, 1933.

In this little book, Dr. Tucker, a physician of wide experience in courts, schools and clinics, makes a plea for the understanding and proper evaluation of that most difficult period of life—adolescence. He rightly calls attention to the work done with infants in clinics for well babies, to the care of children through the medium of schools and social agencies and to the absolute neglect of the adolescent child. At the risk of being trite, one can say that this book is timely. In these days, marked by a rapidly changing social order, it is difficult for adults to see and evaluate things properly. How hard, then, it must be for the adolescent, who, in addition, has problems of his own to solve. The book is a useful compendium of nervous and mental disorders by means of which parents can recognize incipient disease. The comments under each heading indicate that the child should have proper attention and cautions against "soda fountain remedies." The reading of the book by a layman will aline him with the adolescent and enable him to understand things which have heretofore been regarded only as pernicious and mean. The book would be of especial value to a parent who was having trouble with a growing boy or girl.

La ponction cisternale. By M. R. Castex and L. E. Ontaneda. Translated from the Spanish by G. S. Hardy. La pratique médicale illustrée. Price, 67 francs. Pp. 67, with 22 illustrations. Paris: Gaston Doin & Cie, 1934.

This monograph is devoted to all phases of the subject of cisternal puncture. The anatomy of the cisterna magna and the parts surrounding it is well described and illustrated. The various accidents which have resulted from cisternal puncture are recorded and analyzed. Manometric, cytologic and chemical studies of the fluid obtained from the cistern are compared with those of fluid from the lumbar region. The indications for cisternal puncture are reviewed, and are, on the whole, conservative. The authors give their technic for carrying out the puncture, which is based on careful anatomic study and measurements. They recommend drawing the shortest possible line from the tip of one mastoid to that of the other and using the middle of this as the point of entry of the needle. In the plane of the line so drawn the possibility of injury to vessels is minimized, and if by mischance the needle encounters nerve tissue it will be below the respiratory center. The actual depth of the puncture may be ascertained by measuring with a square the distance from the vertical plane of the tips of the mastoids to the site of puncture and subtracting 2 cm.

Criminal Law in Action. By John Barker Waite, Professor of Criminal Law and Practice, University of Michigan Law School. Cloth. Price, $3. Pp. 321. New York: Sears Publishing Company, 1934.

This book, which was written for the layman, consists of short chapters dealing with the various phases of the legal machinery of this country and places stress on its failures rather than on the actual mechanism of the law itself. The author succeeds in putting his finger on most of the well known weaknesses, such as the system of trial by jury and the manners, methods and attitudes of the police, lawyers, judges, newspapers and the public. The book is not a critique born of experience, nor does it cite specific and apt examples, as does Moley's work in the same field. It is rather a group of examples taken from the criminal history to exemplify the poor working of the legal system. One chapter which might be of interest to the psychiatrist is a rather weak disquisition on insanity as a defense, in which the author gives a lucid but too abridged explanation (from the lawyers' point of view) of all the difficulties which psychiatrists have had to face in their dealings with the courts. Waite probably would have written a different book had he had much contact with criminals.

Behavior Mechanisms in Monkeys. By Heinrich Klüver. Behavior Research Fund Monographs. Price $4. Pp. 387. Chicago: University of Chicago Press, 1933.

Klüver's monograph extends research on animal behavior to new and extremely interesting problems. His work is noteworthy for the excellent technics he uses, and particularly for the "method of equivalent stimuli," which consists essentially of establishing a differential response to one set of stimuli and introducing changes in the stimulus situation with tests to determine whether it is then equivalent or nonequivalent. Among other tests used are various significant experiments in the monkey's use of tools to secure food. Klüver is cautious in interpreting the results, but they represent an advance in the knowledge of behavior mechanisms in monkeys which should receive the careful attention of all students of human as well as of animal behavior. The work shows clearly that the responses of macaque monkeys are much more nearly like those of the anthropoid apes than has usually been supposed. Klüver makes the interesting suggestion that his technics can be applied in experimental work with children and in cases of senile and other forms of mental deterioration.

Neuroanatomy. By J. H. Globus, B.S., M.D., Associate Professor of Neuropathology and Neuroanatomy, New York University and Bellevue Hospital Medical College. Sixth edition, revised and enlarged. Pp. 240, with 89 illustrations. Baltimore: William Wood & Company, 1934.

The sixth edition of this guide for the study of the form and internal structure of the brain and spinal cord appears in a new and enlarged form. The book is arranged in two parts. Part 1 consists of descriptive text and directions for the student's work, arranged in twenty-three assignments. This is illustrated with thirty-six figures from photomicrographs and semischematic drawings. In part 2 are fifty-three plates of outline drawings, which the student is to fill in. Instead of the loose-leaf arrangement previously used, the plates are perforated near their attached borders, so that they can be taken out when the drawings are being completed. Then they can be reattached by strips of adhesive paper, so that the student has a permanent record of his work. This method of study tends to shorten the time necessary to record the structures seen—an important factor in teaching in these days of crowded rosters.

Localization of Function in the Cerebral Cortex: An Investigation of the Most Recent Advances. Volume XIII. Association for Research in Nervous and Mental Disease. Price, $8. Pp. 667. Baltimore: Williams & Wilkins Company, 1934.

Volume XIII of the "Localization of Function in the Cerebral Cortex" is one of the best of the publications issued under the auspices of the Association for Research in Nervous and Mental Disease. The scheme of the book is good. There are three sections: (1) anatomic basis; (2) physiologic analysis, and (3) clinical studies. It is rather difficult to review such a book, because it contains so many excellent papers which merit separate analysis. Suffice it to say that it is a creditable production. It is also obvious that the annual meetings of the Association for Research in Nervous and Mental Disease, so far as their products are concerned, have turned out well.

Hirnpathologische Beiträge. By Prof. K. Schaffer and Prof. D. Miskolczy. Volume 13. Pp. 500. Budapest, Hungary: K. Schaffer, 1933.

This volume is the thirteenth series (1933) of works from the clinics of Schaffer and Miskolczy in Budapest and Szeged. It is composed of reprints representing the output from these clinics during 1933. The researches cover fields of normal neurohistology, neuropathology and clinical neurology and psychiatry. Among the contributions are studies of the cerebellar cortex of the rabbit, the development

of microglia, the pathogenesis of primary systemic nervous diseases, the pathogenesis of amaurotic family idiocy, studies on the visual tracts and fibers, poliomyelitis posterior, syphilitic meningitis, epilepsy, the syndrome of the corpus Luysii, hemitorsion dystonia, schizophrenia and other subjects. The standards set by the heads of these well known clinics have been well retained and exemplified by these latest works of both leaders and students.

Aufbau und Abbau der Grosshirnleistungen und ihre anatomischen Grundlagen. By Max de Crinis. Price, 7.80 marks. Pp. 95, with 15 illustrations. Berlin: S. Karger, 1934.

In the first section of this monograph, on the morphologic basis of mental development, de Crinis includes a report of his studies of the brains of sixty-eight children, showing the growth of ganglion cell dendrites at different ages. The remainder of the book contains no original material, but is a concise presentation of the classic views on the development of mental activities, their deterioration following cerebral lesion and the site and nature of the lesions underlying different syndromes. In the fields of aphasia, apraxia and agnosia de Crinis lays greatest stress on the doctrines of Wernicke; he refers to some of the newer points of view, but briefly and with little critical analysis.

Die Wirbelgelenke. Supplementary volume to the Zeitschrift für orthopädische Chirurgie. Volume 61. By Max Lange. Price, 7 marks. Pp. 117 plus, with illustrations. Stuttgart: Ferdinand Enke, 1934.

This monograph is chiefly devoted to the roentgenologic diagnosis of diseases of the vertebral articulations. By a special technic it is possible to display the articular spaces and surfaces of each side separately at various levels. A detailed description is given of the normal appearances, and pathologic alterations are illustrated both in x-ray films and in actual pathologic specimens. There are also brief notes on the clinical aspects of various diseases of the joints. The treatise is particularly intended for those interested in the orthopedic treatment of diseases of the spinal column, but there is also much of neurologic interest. It is well printed and illustrated.

Aids to Neurology. By E. A. Blake Pritchard, M.A., M.D., Cambridge; M.R.C.P. Price, $2. Pp. 376. Baltimore: William Wood & Company, 1934.

This book is intended for the use of students in the early years of their medical training. It is, however, a fairly complete presentation from the clinical standpoint. The points of view are those usually adopted. The subject is well presented. On the other hand, it is always a question whether these small books or compends fulfil the expectations of the author, for usually students desire something much more comprehensive.